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SEPTEMBER 1954
VOLUME 70 NUMBER 3

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Oct. 30, 1917, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

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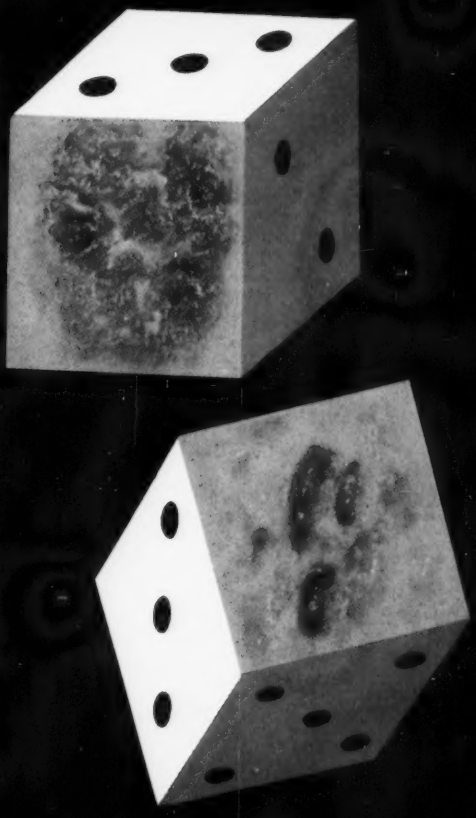

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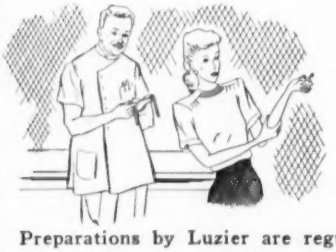

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VOLUME 70 SEPTEMBER 1954 NUMBER 3

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PERSONALITY AND EMOTIONAL FACTORS IN CHRONIC DISSEMINATED NEURODERMATITIS

CLAUDE E. FISKE, Ph.D.
AND
MAXIMILIAN E. OBERMAYER, M.D.
LOS ANGELES

THE IMPORTANT role of psychic factors in chronic disseminated neurodermatitis is recognized widely. Elucidation of the precise nature and relationships of the factors involved, however, still is to be accomplished. As a step in this direction an exploratory study of patients with the disease has been carried out during the last three years.

Some of the observations already have been published.[1] These data suggested that, while a psychologic structure common to all of the subjects with chronic disseminated neurodermatitis could not be determined, certain characteristics appeared to be significant, for example, a tendency to turn hostile or aggressive impulses inward, a propensity to bottle up emotions, and a strong concern with tactile sensations and touch.

The present report is concerned with comparing personality factors in patients with neurodermatitis and in neurotic patients as revealed through a series of psychologic tests. The aim of this phase of the study was to determine whether or not any particular pattern or cluster of personality traits could be demonstrated in either of these two groups of patients.

The subject group comprised 21 patients with chronic disseminated neurodermatitis under treatment at the Veterans Administration General Medical and Surgical Hospital, Long Beach, and a control group of 21 neuropsychiatric patients at the Veterans Administration Mental Hygiene Clinic, Los Angeles, and the Neuropsychiatric Hospital, Veterans Administration Center, Los Angeles. All were Caucasian men, veterans of the Armed Services; their ages ranged from 24 to 50 years. The controls were matched with the subjects as to age, race, intelligence, education, duration of symptoms, period of hospitalization, and social-economic status.

In the subject group the diagnosis of chronic disseminated neurodermatitis was made by two or more dermatologists, including one of us (M. E. O.); in every instance it was the only disorder, patients with other physical or neuropsychiatric disease being excluded. The controls had been classified as follows: anxiety reaction 9, depressive reaction 3, dissociative reaction 1, conversion reaction 2, obsessive-compulsive reaction 3, phobic reaction 3.

The tests employed were the Rorschach, the Draw-a-Person, the Thematic Apperception, and the Shipley-Hartford; a biographical data sheet compiled by one of us (C. E. F.) also was utilized. All patients were given the psychologic tests individually. The results were scored and these data, after routine removal

TABLE 1.—*Personality Characteristics Investigated in Patients with Neurodermatitis and in Neurotic Persons*

	A	B		C	
	Values According to Tschuprow's Coefficient †	Items Differentiating Within Group with Neurodermatitis ‡		Items Differentiating Within Neurotic Group ‡	
		Direction	Level of Significance	Direction	Level of Significance
1.* Compulsive character structure	....	..	....	..	....
2. Hysterical character structure	0.48	..	....	—	0.05
3. Mixed hysterical-compulsive character	0.49	—	0.01	—	0.01
4. Anal-phallic constellation (i. e., phallic level with residuals of destruction and violence)	0.48	..	....	—	0.01
5. Self-absorption	0.62	#	0.01	#	0.01
6. Superficial social conformity	0.69	#	0.01	#	0.01
7. Emotional spontaneity	0.69	—	0.01	—	0.01
8.* Labile emotionality	....	..	....	..	....
9. Anxiety	0.74	#	0.01	#	0.01
10.* Depression	....	..	....	..	....
11. Above average I. Q.	0.75	..	....	..	....
12. Concrete intelligence	0.58	..	....	..	....
13. Exceptional ambition	0.50	..	....	#	0.01
14. Ambition outstrips abilities	0.48	..	....	—	0.01
15. Fear of external world	0.48	#	0.01	..	....
16. Obsessional sense of injustice	0.67	—	0.01	—	0.01
17.* Paranoid features	....	..	....	..	....
18. Feeling of being hemmed in by social environment	0.62	#	0.05	..	....
19. Strong hostile-dependent relationship to parent	0.54	#	0.01	#	0.05
20. Hostility close to surface	0.52	..	....	..	....
21. Hostility toward family	0.69	#	0.01	#	0.01
22. Guilt over hostile impulses	0.63	#	0.01	#	0.05
23. Low stress tolerance	0.70	#	0.01	#	0.01
24. Abnormal preoccupation with contact in form of fear of being touched	0.48	..	....	..	....
25. Deep-seated feeling of insecurity	0.64	#	0.01	#	0.01
26. Feeling of rejection by strong parent	0.60	#	0.01	#	0.01
27. Self-pity	0.58	#	0.01	..	....
28. Unsatisfied need for affection	0.72	#	0.01	#	0.01
29. Conflict over dependency needs	0.70	#	0.01	#	0.01
30. Maso-exhibitionistic discharge of hostility and guilt	0.48	..	....	—	0.01
31. Difficult interpersonal relationships	0.55	#	0.01	#	0.01
32. Narcissism	0.48	#	0.01	..	....
33. Exhibitionistic desires	0.50	#	0.05	..	....
34. Masochistic desires	0.48	..	....	—	0.01
35. Voyeurism	0.49	..	....	—	0.01
36.* Rejection of sexual role	....	..	....	..	....
37. Masturbation conflict	0.58	#	0.05	..	....
38.* Severe reprisals for masturbation in childhood	....	..	....	..	....
39. Erotization of skin	0.49	#	0.05	—	0.01

* Unreliable items (a value for Tschuprow's coefficient lower than 0.48, i. e., less than 77% agreement of three judges).

† Tschuprow's coefficient: $T^2 = \dfrac{\dfrac{X^2}{N + X^2}}{1 - \dfrac{X^2}{N + X^2}}$

‡ Lowenstein's tables of significance (Moses, L. E.: Non-Parametric Statistics for Psychological Research, Psychol. Bull. **49**: 122, 1952).

\# Present.

— Absent.

of identification, were submitted to three competent clinical psychologists, staff members of the Veterans Administration, who judged the material independently. Every patient was rated on 39 items that embraced personality, emotional and intellectual characteristics of significance in neurodermatitis and in neuroticism as derived from the literature. The judges rated the items as "strongly present," "present," "cannot say," or "absent." Each item, therefore, received 126 ratings (three judgments on each of the 42 patients). The total ratings of the 39 items, 4,914 in all, constitute the raw data evaluated statistically.

Nonparametric or distribution-free statistical methods were employed. The reliability of the various items was determined by a measure of contingency, Tschuprow's coefficient [2] (Table 1, Column *A*). Any item on which the judges did not agree in at least 97 of the 126 judgments (77%) was eliminated from further statistical consideration.

The presence or absence of any characteristic within the subject group or within the control group and the items differentiating these two groups at a level

TABLE 2.—*Items Differentiating Between the Neurodermatitic and Neurotic Groups.*

		Direction	$\frac{D^2}{\Sigma D^2}$ =	$\frac{(P_1 - P_2)^2}{\frac{PQ}{N_1} + \frac{PQ}{N_2}}$	Level of Significance
4.	Anal-phallic constellation	# in N.D.		4.86	0.05
13.	Exceptional ambition	# in controls		6.02	0.02
22.	Guilt over hostile impulses	# in N.D.		3.85	0.05
24.	Abnormal preoccupation with contact in form of fear of being touched	# in N.D.		9.00	0.01
30.	Maso-exhibitionistic discharge of hostility and guilt	# in N.D.		6.13	0.02
32.	Narcissism	# in N.D.		3.87	0.05
34.	Masochistic desires	# in N.D.		6.89	0.01
35.	Voyeurism	# in N.D.		3.90	0.05
37.	Masturbation conflict	# in N.D.		4.50	0.05
39.	Erotization of skin	# in N.D.		11.08	0.01

Present.

of significance equal to or better than 0.05 were determined by means of Worthing and Geffner's formula, "Difference between Two Proportions." [3]

Constellation analysis,* a new statistical method, was applied to the data in an attempt to determine which, if any, characteristics coexisted exclusively in the patients with neurodermatitis, or exclusively in the neurotic patients, or whether the whole group had any such linked traits in common.

Individual items differentiating within each group are presented in Table 1, Columns *B* and *C*. Nine characteristics peculiar to the patients with neurodermatitis were statistically significant in discriminating these subjects from the neurotic patients (Table 2). Of particular interest is the fact that two characteristics frequently referred to in the literature as typical of the personality of the patient with neurodermatitis, namely mixed hysterical-compulsive character and obsessional sense of injustice, were significantly absent in our group of such patients. On the other hand, our analysis corroborates the conclusions of many other investigators that the patient with neurodermatitis has many characteristics of personality that are psychopathologic: Thirteen individual traits were determined to be

* Gengerelli, J. A.: Unpublished paper, University of California at Los Angeles, 1952.

common to both subjects and controls (Table 3). These data suggest that the patients with neurodermatitis constitute a subgroup of the neurotic population in general.

TABLE 3.—*Items Yielding Common Results in Both Patients with Neurodermatitis and Neurotic Patients*

	Direction *
3. Mixed hysterical-compulsive structure	—
5. Self-absorption	#
6. Superficial social conformity	#
7. Emotional spontaneity	—
9. Anxiety	#
16. Obsessional sense of injustice	—
19. Strong hostile-dependent relationship to parent	#
21. Hostility toward family	#
22. Guilt over hostile impulses	#
23. Low stress tolerance	#
25. Deep-seated feeling of insecurity	#
26. Feeling of rejection by strong parent	#
28. Unsatisfied need for affection	#
29. Conflict over dependency needs	#
31. Difficult interpersonal relationships	#

\# Present.
— Absent.

TABLE 4.—*Constellation Analysis of Neurotic Group: Pairs of Items Occurring Together in the Neurotic Personality*

Superficial social conformity	Unsatisfied need for affection
Above average I.Q.	Narcissism
Strong hostile-dependent relationship to parent	Feeling of rejection by strong parent
Hostility close to the surface	Narcissism
Low stress tolerance	Difficult interpersonal relationships
Deep feeling of insecurity	Unsatisfied need for affection
Conflict over dependency needs	Masturbation conflicts

TABLE 5.—*Constellation Analysis of Patients with Neurodermatitis*

Triad:		
Anal-phallic constellation	Low stress tolerance	Difficult interpersonal relationships
Pairs:		
Superficial social conformity		Anxiety
Difficult interpersonal relationships		Anxiety
Abnormal preoccupation with contact in form of fear of being touched		Exceptional ambition
Guilt over hostile impulses		Deep-seated feeling of insecurity
Anal-phallic constellation		Deep-seated feeling of insecurity
Anal-phallic constellation		Feeling of rejection by strong parent
Self-absorption		Masturbation conflict

Coexistent traits common to the entire group were not present. Seven pairs of items were determined for the neurotic control group (Table 4) while, in the patients with neurodermatitis, seven different pairs of items and one constellation of three items were extracted (Table 5).

Several important aspects of differentiation of the group with neurodermatitis from the neurotic group warrant delineation: Perhaps of primary significance is

the observation that the basic personality structure of the patient with neurodermatitis is characterized by a combination of anal and phallic elements. The first confers the features of sadism, masochism, conflicts between aggression and submission, orderliness, obstinacy, rebellion against environment, fears of being trapped and cheated, guilt, rigidity, and the ambivalent relationships that so often characterize patients with neurodermatitis. The phallic component contributes the features of narcissism, open aggression, sensitivity, tendency to emotional lability, exhibitionism, strong feelings of insecurity and doubts about abilities, and sexual confusion with erotization of the whole body. It is the interplay—the variable and inconstant relationships—of these elements of personality that produces the complicated picture in such patients. The coexistence of these two levels of development probably accounts for the confusion between compulsive and hysterical personality structures—a confusion prevalent in the literature. Anal elements make up the major portion of the compulsive personality, while phallic components are commonly found in the hysteric type.

Strong guilt feelings connected with hostility were almost universally present in the patients with neurodermatitis. Guilt is typical of anal-sadistic regression in which the retained superego is unable to tolerate hostile transgressions. The need to relieve such conflict on the environment interferes with the establishment of warm and genuine social relations with others; this may be responsible, in part, for the social difficulties of such patients. A somewhat tangential consideration arises in respect to this feature: If feelings of guilt are so cataclysmic in patients with neurodermatitis, why does suicide so rarely occur in the presence of the disease? It may be postulated that they can relieve their guilt tensions by unconscious expression, through the skin, of both aggression and self-punishment. Furthermore, the phallic component permits more free environmental expression of aggressive impulses so that they need not be turned inward.

The distinctive series of preoccupations and conflicts centering around the skin suggests that, in patients with neurodermatitis, the skin has become a primary medium for expression of conflictual desires, impulses, and needs. For instance, these patients exhibit abnormal sensitivity to, and reaction against, close physical contact; the skin would seem to represent a vulnerable defense against desired, yet feared, close personal relations with others—to constitute a fragile bulwark against the oppressive forces of the environment.

The abnormal importance of the skin is reflected also in its sexualization: It assumes the functions of both expression of and satisfaction of conflictual sexual desires and needs. The factors underlying such transfer of function probably are manifold; those suggested by this study are basic fear of genital sexuality, strong conflict over masturbation operating against normal masturbatory outlets, regression to infantile modes of sexual satisfaction in which warmth and touching of the skin are important, and utilization of the skin as a vehicle for exhibitionistic and sadomasochistic desires—both largely expressions of infantile sexuality.

Closely related to cutaneous erotization is utilization of the skin, by these patients, as an instrument for the satisfaction of masochistic and exhibitionistic desires. In brief, through the medium of pruritic and offensive lesions, the patient satisfies his need for self-punishment and, simultaneously, discharges on his environment hostility by inflicting on others the sight of his repulsive eruption.

These abnormal preoccupations with the skin and its unusual sexual significance immediately pose a thorny problem: When and why did the skin assume its primary role? A categorical answer most certainly is not provided by this study. It does, however, permit speculation: First, regression to pregenital levels of sexuality seems clear: On this infantile level sexual sensitiveness and responsiveness is diffused to the total body covering; the skin is the organ responsive to sexually-determined impulses and desires. Second, satisfaction of the masochistic needs becomes dependent on painful stimulation of the skin; it assumes paramount importance in gratification of these needs. Third, the patient with neurodermatitis is abnormally preoccupied with physical and emotional closeness and, since the skin is the natural barrier between the self and the threatening environment, it takes on a special significance. Fourth, the conflict revealed in these patients between internal and external expressions of strong hostility is at least partially resolved by disgorging it on the region between the self and the outside world, i.e., the skin.

The absence of any particular constellation or of any consistent group of factors in the neurotic patients and the presence of such a constellation in those with neurodermatitis suggest that the neurotic patients are more heterogeneous; this observation reemphasizes the probability that the experimental group may be a special, somewhat homogeneous, subgroup in the total neurotic population. The items that form a constellation in the patients with neurodermatitis, (Table 5) are of interest in that if the anal-phallic cluster is broken down, its component parts contain most of the attributes widely mentioned in the literature in connection with neurodermatitis, namely, sadism, masochism, exhibitionism, aggression, guilt, ambivalent relationships, rigidity, narcissism, sensitivity, insecurity, sexual conflicts, hyperexcitability, and lack of warm, close relationships with others.

CONCLUSIONS

Because of the limited number of patients involved, only tentative conclusions regarding personality and emotional factors in chronic disseminated neurodermatitis may be drawn. This study, however, strongly suggests that such characteristics are of significance in distinguishing patients with the disease from other neurotic persons, and that they probably play an important role in the developmental background of neurodermatitis. Analysis of the data secured by this series of psychologic tests indicates that:

1. The patients with neurodermatitis have many of the psychopathologic traits common to the neurotic population; such patients may be considered a subgroup thereof. These common traits are self-absorption, anxiety, superficial social conformity, lack of emotional spontaneity, hostile-dependent relationships, low stress tolerance, deep-seated feelings of insecurity and rejection, unsatisfied need for affection, and difficult interpersonal relationships.

2. The patients with neurodermatitis are more homogeneous than are those with mixed neurotic diagnosis. The former were determined to have a cluster of personality traits in common.

3. The basic personality structure of the person with neurodermatitis is distinguished by conflictual infantile elements. Sadistic, destructive, paranoid, and

aggressive elements, together with elements of masochism, insecurity, narcissism, sensitivity, dependency, and marked sexual conflicts were demonstrated.

4. The patient with neurodermatitis is distinguished from other neurotic persons by several areas of conflict, primarily by marked preoccupation with the skin and its erotization, and to a lesser degree by such characteristics as guilt over hostility, hostile-dependent relationship to parents, masturbation, and needs for self-punishment and exhibitionism.

5. One important feature of the skin to patients with neurodermatitis is that it constitutes an uncertain barrier between self and baneful environmental forces.

6. Selection of the skin as the site of discharge in the presence of this disease is based on several factors, among which is regression to infantile levels of sexuality with increased sensitivity and responsiveness of the entire body covering.

7. The confusion of compulsive and hysterical attributes reported in the literature may be accountable to a mixture of traits from two levels of personality development, the anal and the phallic.

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MEASUREMENT OF SENSITIVITY OF CUTANEOUS NEVI

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THE HISTOGENESIS of nevi still remains controversial. The epidermal theory of their origin is favored by Block, Miescher, Ormsby, and Montgomery,* who believe that certain basal cells of the epidermis under suitable stimulus assume the ability to produce melanin. This opinion is opposed to the concept of the neurogenic origin of neval cells as conceived by Masson [4] and proposed by Soldan.[5]

Some protagonists of the epidermal origin of nevi have offered in support of their beliefs the clinical opinion that moles are no more sensitive than the rest of the skin, and that they should be, if the neural theory of their origin be valid.

If these pigmented growths have their origin in cells of the peripheral nerve apparatus in the skin, it was considered to be of some interest to see if any variations in sensitivity could be elicited and recorded.

Clinical impressions of the reaction of a nevus to common stimuli vary with the individual observer and are an unreliable index. However, if the relative sensitivity of nevi could be measured quantitatively by laboratory procedures, such a determination might contribute some relevant information. If nevi were found to be more reactive than normal skin, one might assume either that nevi have greater nerve preceptors than normal skin or that in their development they have retained their presumptive relationship to the peripheral nervous system, whereas if they were found to be insensitive or less sensitive, it would favor but not necessarily prove the opposing theory. Therefore, the following experiment was devised to ascertain the relative sensitivity of nevi as contrasted with the normal skin and with other cutaneous growths of different cellular composition located in similar anatomical sites.

METHOD

Qualitative estimation of skin sensitivity have been determined by various methods, i. e., stroking skin with a hair, pin prick, pressure with a probe, and heat. However, since the advent of the Hardy, Wolff, and Goodell [6] Dolorimeter (Figure), and the thermal radiation method designed by them, it has been possible to make quantitative determinations of the pain threshold of the skin. Their technique was employed in these experiments. Because of the influence of skin temperature upon pain evoked by thermal stimulation, the skin temperature was measured with a Hardy dermal radiometer before each measurement of pain threshold or pain intensity.

From the Mixed Tumor Service, Memorial Center for Cancer and Allied Diseases.

* References 1 to 3.

The thermal stimulus was produced on the skin by a three-second exposure to the rays from a 500-watt incandescent lamp, which was focussed on the area to be tested. The test areas were blackened with India ink to insure complete absorption of the radiation and to prevent effects due to penetration of the rays below the skin surface. Thus the stimulus was purely a thermal one.

Measurement of Pain Threshold.—In testing the pain threshold, the subject reported on the sensation experienced at the end of the three-second exposure, and the stimulus intensity evoking the least perceptible pricking pain was considered to be the pain threshold. Satisfactory results were obtained by approaching the pain threshold from below, i. e., with two or three weaker stimuli. This prevented overstimulation of a test area and subsequent hyperalgesia. Measurements were made on the tumors and on an adjacent area of unaffected skin.

Measurements of Pain Sensibility.—In testing sensibility of the tumors and normal skin to pains above the threshold, a stimulus evoking a pain of 5-dol intensity [7] was administered on the tumor. Then an attempt was made to find the degree of stimulation required to elicit a pain of like intensity in the adjacent normal skin by presenting stimuli of various intensities until the subject was able to say that one of the them produced a similar pain.

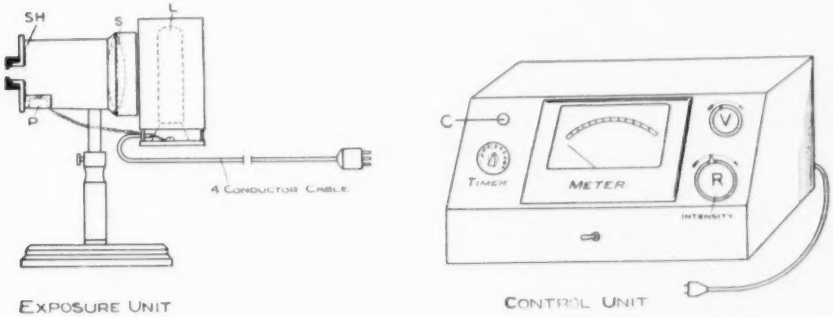

Diagram of the Hardy-Wolff-Goodell pain threshold apparatus used in these experiments. *P*, electronic shutter set at 3 seconds; *S*, short focus lens; *L*, 500-watt lamp. Control unit contains intensity controls, a meter for reading stimulus intensity, and exposure switches. (Courtesy of Dr. James Hardy.)

Subjects.—The subjects included 16 patients who presented themselves with nevoid and other cutaneous growths. The nevi and other growths varied in contour, color, size, and anatomical distribution on the skin. Pathologic diagnosis was obtained in all instances.

Of the 16 cases, there were 11 nevi, 1 melanoma (included with the nevi in the table of results), 1 sclerosing angioma, 1 xanthoma, and 2 multiple neurofibromas (von Recklinghausen's disease). In some patients suitable comparisons of pain sensitivity could not be made on the skin because of the location of the growth or because the patient became too upset to cooperate properly. The findings on these patients were not included in the final results.

RESULTS

The results of the measurement of pain threshold and pain sensitivity on the nevi and other cutaneous growths are given in Table 1.

Pain Threshold.—In 12 patients with nevi (including one melanoma) in whom the pain threshold was measured, three of the nevi showed values above normal; four were unchanged, and of the remaining five, the threshold was lower on the nevus than on the adjacent skin; while in the 4 patients with growths other than

nevi, there were 2 in which the threshold on the growth was increased, and 2 in which the threshold on the growth was unchanged. None of the non-neval growths showed a decreased threshold.

Pain Sensitivity.—Comparison of pain sensitivity showed 9 of the 12 nevi to have increased pain sensitivity as compared with the adjacent skin; in 2, the pain sensitivity was unchanged; and in 1, it was decreased on the nevus. In the four non-neval growths, pain sensitivity on the growth was decreased or unchanged in all four.

TABLE 1.—*Results of Measurement of Pain Threshold and Pain Sensitivity on Dermal Nevi and Other Dermal Growths*

		Pain Threshold			Pain Sensitivity		
Skin Site	Pathologic Diagnosis	Unchanged	Increased	Decreased	Unchanged	Increased	Decreased
Foot (Dorsum)	Jadassohn-Tiesche nevus	..	..	X	..	X	..
Chest	Compound nevus	X	..	..	..	X	..
Forearm	Jadassohn-Tiesche nevus	..	..	X	..	X	..
Finger (Dorsum)	Compound nevus	X	..	..	..	X	..
Leg	Jadassohn-Tiesche nevus	..	..	X	..	X	..
Arm	Plexiform neuroma	X	..	..	..	..	X
Arm	Plexiform neuroma	..	X	..	..	..	X
Back	Dermal nevus	..	X	..	..	..	X
Hand	Jadassohn-Tiesche nevus	X	..	..	..	X	..
Leg	Melanoma	..	X	..	..	X	..
Arm	Sclerosing angioma	X	..	..	X	..	..
Arm	Dermal nevus	X	..	..	..	X	..
Heel	Compound nevus	..	..	X	..	X	..
Foot (Dorsum)	Compound nevus	..	X	..	X	..	..
Back	Intradermal nevus	..	..	X	X	..	..
Leg	Xanthoma	..	X	..	X	..	..

TABLE 2.—*Comparison of Results of Measurement of Pain Threshold and Pain Sensitivity in Dermal Nevi with Other Dermal Growths*

		Pain Threshold			Pain Sensitivity		
Type of Growth	No. Cases	Unchanged	Increased	Decreased	Unchanged	Increased	Decreased
Nevi (1. Melanoma)	12	4	3	5	2	9	1
Sclerosing angioma	1	1	..	..	1	..	..
Plexiform neuroma (von Recklinghausen)	2	1	1	..	..	..	2
Xanthoma	1	..	1	..	1	..	..

COMMENT

In the above 16 cases, 8 with lowered or unchanged thresholds showed increased sensitivity to higher stimuli when compared with the adjacent skin. In four others in whom the threshold was elevated, sensitivity was unchanged or decreased; in the remaining four patients, one had an increased sensitivity with raised threshold; in one both sensations were unchanged; in one the threshold was unchanged and sensitivity decreased; in one, the threshold was lowered and the sensitivity unaltered. In no instance was the threshold lowered and the sensitivity decreased.

In Table 2 there is a comparison of results of the measurement of pain threshold and pain sensitivity between the dermal nevi and the other cutaneous growths. It will be seen that none of the non-nevoid growths showed evidence of increased pain sensitivity or decreased pain threshold; 9 of the 12 nevi showed a definite increase of sensitivity in comparison with the surrounding normal skin. From these disclosures one would infer that there was some nerve element present in these neval growths that was not present in the adjacent skin or a component of other dermal growths of different histologic background, but arising in anatomical sites on the skin similar to that of the nevi.

It is interesting that the neurofibromas of von Recklinghausen should show no evidence of increased sensitivity. Their probable origin from the proliferation of the neural sheath rather than a Schwannian nerve component, as in the case of the nevi, and the differences in the ratio of the fibrous tissue component together with the full thickness of cutis overlying the tumor may account for this somewhat paradoxical finding.

The cutis is innervated by a branching plexus of nerve fibers following for the most part the course of the arterial vessels. As they progress from the deeper portion of the dermis toward the epidermal surface, there is a gradual decrease in their caliber, and in their course they branch off to glands and muscle, finally terminating on the surface of the hair follicle, in the arrectores pilorum, or in tactile corpuscles, or in the papillary layer, or the epidermis. They contain myelinated as well as Remak's fibers. At their entrance into the dermis they are surrounded by a stratified perineurium composed of several sheaths. As their caliber decreases, there is only a single sheath—the sheath of Henle. The majority of the dermal fibers appear to have a sensory function. Certain of these dermal nerve fibers traverse the neval tissue, terminating in normal fashion, while other nerves pierce the tissue of the nevus and are affected in a variety of ways.

Masson [8] considers all nevi (with rare exception) to originate from the proliferation of the Schwannian cells of these dermal nerves in combination with coexisting reproduction of the intraepidermal melanoblasts. From a fusion of these two elements the neval tissue is formed. The nerve endings in the dermis differentiate to form the lamé foliacée, laminated nerve formations in the dermis that resemble the tactile Wagner-Meissner corpuscle and in the epidermis corpuscular bodies simulating those of Merkel-Ranvier.

Masson's identification of caricatures of Meissnerian tactile corpuscles in nevi has been corroborated by Stout,[9] Ewing,[10] and Foot.[11]

From a phylogenetic aspect, pigmented hairy moles in man have been viewed as animal vestiges of tactile, mammalian hairs by Henneberg,[12] Friedenthal,[13] Sklarz,[14] and Sulc.[15] In support of this idea, Laidlaw and Murray[16] demonstrated the striking resemblance between human moles and the tactile spots of reptiles (alligators). They presented the phylogenetic and ontogenetic hypothesis that in the course of evolution the reptilian tactile spots were replaced by mammalian hair follicles. Subsequently there appeared a transition between the pigmented tactile spot of the reptilian type and the hair tactile organ of the mammalian type in the form of the congenital mole of the human. In all instances this was a local variation of the same fundamental or original neuroectodermal tissue.

In this same respect the mole has been considered a progonoblastoma, rather than a peculiar aberration in the developmental growth of the embryo, i. e., a vestigal phylogenetic tumor. Ribbert [18] considered this postulate in a description of a pigmented mole of the skin, as did Jendralski [19] in presenting a conjunctival nevus.

More recent work of Masson [8] and Becker [17] supports the concept that the melanoblastic neval cells of human epidermis may originate from the neural crest, as in the case of the pigment-forming cells of lower animals. The exceptions in which Masson excludes the neural origin of nevi are those nevi of palmar or plantar origin, leucoderma centrifigum asquisitum and junction nevi. He considers junction nevi as arising from the intradermal melanoblasts, whose neuroectodermal origin has of course been equivocal. Recent embryologic studies, however, support the concept of their origin from the nervous system.†

If the neural histogenesis of these nevi be true, then one might anticipate some difference in the sensitivity in these neval growths as compared with normal skin such as has been suggested by the results of this investigation. On the other hand, the demonstrated increased sensitivity of these nevi indicates that they are abundantly supplied with sensory nerve fibers, which could be coincidental and does not necessarily add proof to the hypothesis of a neurogenic origin, although it is suggestive.

SUMMARY AND CONCLUSION

The results of the measurement of pain threshold and pain sensitivity would indicate that nevi are more sensitive than the normal skin and more sensitive than other cutaneous growths in similar anatomical sites on the skin.

A paradoxical finding was made of the absent or decreased sensitivity of multiple neurofibroma of the skin (von Recklinghausen's disease).

Laboratory determinations were made in the Department of Physiology, Cornell Medical School, through courtesy of Dr. James Hardy with technical assistance of Margaret Meixner.

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LICHENOID ERUPTIONS

A Histopathological Study

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THE LICHENOID eruptions are a challenge diagnostically, to both the clinician and the histopathologist, especially in dermatoses which have a lichenoid phase. This clinical uncertainty is usually the result of similar changes in the gross histopathologic structure. However, on correlating the more minute and detailed microscopic findings with the clinical picture one can differentiate this group of dermatoses.

REVIEW OF LITERATURE

These eruptions have most frequently been reported as atypical lichen planus. One form has been named lichen planus erythematosus.* Lortat-Jacob,† in a discussion of a case of this type presented by Gougerot, thought the lichenoid eruption was secondary to arsenic used in the treatment of this patient for syphilis. Quinacrine (Atabrine), prescribed for the suppression of malaria during World War II, produced many cases of lichenoid eruptions.‡ Clinically these lesions were similar to lichen planus in type of lesion, distribution, course of the disease, and sequelae. At times, lupus erythematosus was simulated clinically with the formation of scaly plaques that healed leaving epidermal atrophy. Histologically, these lesions were reported as indistinguishable from lichen planus.

Dowling's case, presented by Meara,[18] was clinically and histopathologically lichen planus. This patient previously had been treated with gold for rheumatoid arthritis. Schwartz,§ in discussing this case, stated that spectrographic examinations of biopsy material of his case revealed deposition of gold in the sections which were microscopically lichen planus.

Gougerot and Civatte [19] described the clinical and the histological variations in lichen planus. They were uncertain as to whether lichen planus was a distinct cutaneous disease or a dermatologic syndrome on a special terrain secondary to diverse etiologic agents. Neither clinical nor histological criteria must be considered as characteristic separately, but rather they must be studied together for the correct diagnosis, and they emphasized that for best histologic evaluation it was necessary to study lesions with minimal changes. They were at times unable to differentiate microscopically lichen planus, lupus erythematosus, and poikiloderma.

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* References 1 to 7.

† Lortat-Jacob, in discussion of Gougerot and Blum.[9]

‡ References 10 to 17.

§ Schwartz, B., in discussion of Meara.[18]

Shatin, Canizares, and Worthington [20] reported the occurrence of lichen-planus-like eruption in five cases following the use of paraaminosalicylic acid in the treatment of pulmonary tuberculosis. Two of their cases were diagnosed as lichen planus on histologic examination. In one of these cases parapsoriasis was also considered histologically.

REPORT OF CASES

CASE 1.—G. B., a 53-year-old white man, entered the hospital because of dermatitis which involved the extensor and flexor surfaces of both forearms.

Just prior to the eruption this patient had suffered a coronary vascular occlusion for which he was treated with quinidine, aminophylline and phenobarbital.

Physical examination revealed a reddish-purple maculopapular eruption covering the flexor and extensor surfaces of both forearms. Microscopic section of a hematoxylin-and-eosin-stained typical lesion (Figs. 1 and 2) reveals slight hyperkeratosis, zonal granulosis, and obliteration of the epidermal pegs by colliquative degeneration of the basal cells. The infiltrate, predominantly of round cells, is sharply marginated on its lower border. The upper portion is pressed up against the basal layer. The infiltrate contains histiocytes laden with melanin. Hair follicles are present and appear normal. The histologic diagnosis was lichen planus.

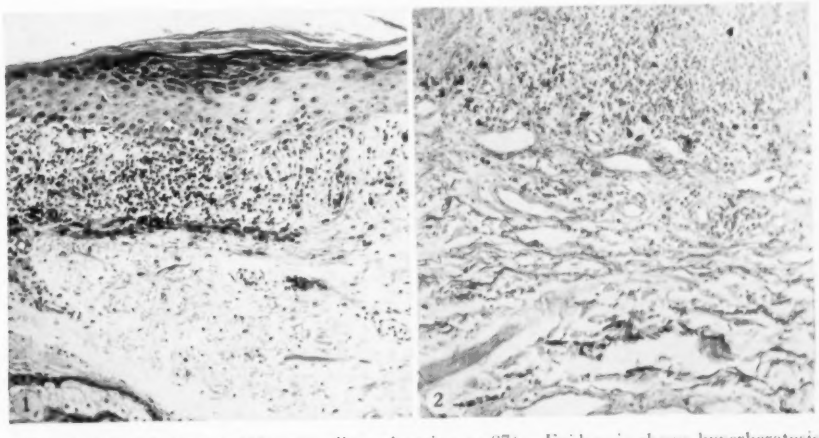


Fig. 1. (Case 1, G. B.) (Hematoxylin and eosin; × 87).—Epidermis shows hyperkeratosis, granulosis, and colliquative degeneration of basal cells. Infiltration consisting of histiocytes and lymphocytes seen in the upper cutis. Smooth muscle and sebaceous glands present and normal.

Fig. 2. (Case 1, G. B.) (Elastic stain; × 87).—Elastic fibers are absent from the upper cutis. Round cell infiltration studded with numerous melanin-bearing histiocytes are seen. There are dilated vessels at papillary cutis. Elastic fibers are present in normal amounts in mid and lower cutis.

CASE 2.—E. Z., a 42-year-old white man, first noted an erythematous papule on the tip of his nose six months prior to hospitalization. Dermatitis subsequently spread over the nose, cheek, and chest. No history of previous illness or ingestion of drugs was elicited. Physical examination revealed an erythematous-keratotic scaling dermatitis with confluent infiltrated patches over the butterfly area of the face and sternum.

Microscopic examination of the histologic sections (Fig. 3) showed a mild hyperkeratotic and parakeratotic process, with regional granulosis and diffuse colliquative degeneration of the basal cells with areas consisting of lymphocytes. There are many melanin-containing histiocytes in the upper cutis. The vessels and the lymphatics are dilated. The sebaceous glands and hair follicles are present. The ostia of the follicles are plugged with keratin. Elastic stained sections (Fig. 4) indicate an absence of elastic fibers in the upper cutis in the areas of the infiltrate.

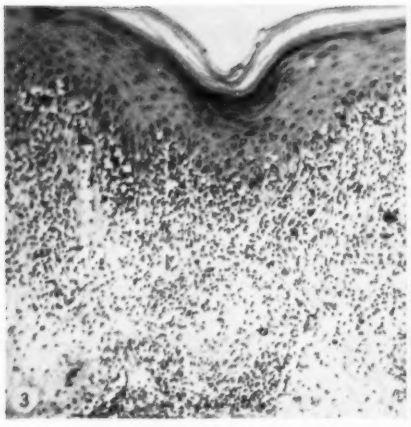
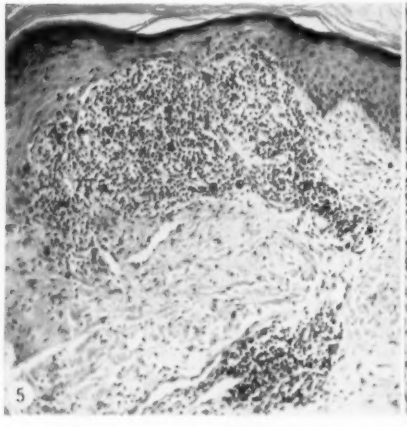


Fig. 3. (Case 2, E. Z.) (Hematoxylin and eosin; × 87).—Epidermal changes are mild hyperkeratosis, follicular granulosis, and colliquative degeneration of basal cells. The epidermal cutis junction although undergoing colliquative degeneration is distinct. The infiltrate is perivascular and localized in the papillary and reticular cutis.

Fig. 4. (Case 2, E. Z.) (Elastic stain; × 130).—Elastic fibers are absent from the upper cutis but increased in amount in mid cutis.



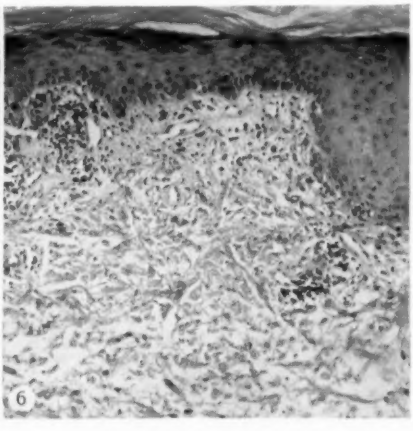


Fig. 5. (Case 3, C. S.) (Hematoxylin and eosin; × 73).—Hyperkeratosis, granulosis, and a sharply demarcated epidermocutis junction are seen. The infiltration consists of round cells and is perivascular. There are no adnexae seen.

Fig. 6. (Case 3, C. S.) (Hematoxylin and eosin; × 73).—Epidermal changes consist of hyperkeratosis, thinning of the epidermis, and a sharply demarcated epidermocutis junction.

In the middle and lower cutis, normal-looking elastic fibers are present. Mallory stains showed a paler-staining collagen in the upper cutis. Histologic diagnosis was chronic discoid lupus erythematosis, although lichen planus could not be ruled out.

CASE 3.—C. S., a 56-year-old white man, first noted an eruption on the dorsa of both forearms which within six months spread to face, ears, and hands. The lesions were pruritic. His history indicated the ingestion of digitalis, phenobarbital, and "pain and sleeping pills" for coronary vascular disease.

The eruption of discrete grouped flat-topped crimson papules formed erythematous plaques with shiny scales on the face, ears, forearms, and hands. The serologic test for syphilis and the lupus erythematosus "Hargraves" cell test were normal.

Specimens were removed for biopsy from typical lesions of the face and forearms. The hematoxylin-and-eosin-stained section from the face (Fig. 5) shows hyperkeratosis, granulosis, and acanthosis. A dense round cell infiltrate is in close approximation to the basal cells which are undergoing colliquative degeneration. The lower border of demarcation of the infiltrate is a straight line. Perivascular infiltrate consisting of lymphocytes, a few polymorphonuclear leucocytes and histiocytes containing melanin extends into the lower cutis.

Fig. 7. (Case 3, C. S.) (Elastic stain; × 73).—The epidermis is atrophied. There is absence of elastic fibers from the upper cutis and in areas of perivascular infiltration. Increased amounts of elastic fibers are seen in mid cutis.

The histologic section from the arm stained with hemotoxylin and eosin (Fig. 6) shows hyperkeratosis and follicular plugging of the epidermis. The epidermal rete is of normal thickness. The epidermal pegs are obliterated by colliquative degeneration. A narrow band of almost pure lymphocytic infiltrate in the papillary cutis hugs the lower border of the epidermis.

The elastic-stained sections of the above specimens (Fig. 7) show no elastic fibers in the zone of infiltrate. Beneath the zone of infiltrate, the elastic fibers are condensed to form bands and are increased in amount.

COMMENT

Lichen planus must be considered in the differential diagnosis when an eruption is clinically violaceous, papular, and chronic. In order to adequately discuss the lichenoid eruptions one must have a clear-cut definition of such loosely used terms as lichen and lichenification. The group of lesions to which the term lichen is most properly applied is that group in which the papular character of the eruption persists, and, although new lesions appear, the primary lesion once reaching its develop-

mental peak does not change to another type of lesion. Lichenification however, is accepted as a term indicating clinical characteristics such as thickening of the skin, deepening of the skin furrows, accentuation of the skin markings, and loss of elasticity.

The lichenoid eruptions can be classified on the basis of etiological agents into toxic, biologic, chemical, and idiopathic.

The toxic group consists of bacterial agents; staphylococci, acid-fast bacilli, fungi, and spirochetes. In this group we find the "id" eruptions such as bacterid, trichophytid, leukamid, lymphogranulomatid, syphilid, and tuberculid. Besides having the definite similarity clinically of a primary focus with a generalized dissemination by the blood stream, these lesions, with the exception of the leukamid and lymphogranulomatid, all undergo necrotic changes, exudation, and crust formation.

The bacterid and trichophytid resemble each other most closely. Related to the bacterid is miliaria rubra, which O'Brien [21] and Shelley [22] have shown to be bacterial in origin.

The tuberculids are either lichen scrofulosorum, papulonecrotic tuberculid, or the lichen tuberculid. The lesions of lichen scrofulosorum may show crusting which is due to a follicular exudation and has been labelled "eczema scrofulosorum." These lesions are transitory. The papulo-necrotic tuberculid is a larger lesion and always exhibits a central plug which on healing leaves a depressed, pitted scar. Both of these lesions appear in crops. The lichenoid tuberculid,[23] where the allergy and immunity are both high histologically, shows less tendency to necrosis, yet clinically it has the lichenoid appearance.

The syphilid clinically and histologically resembles the tuberculid. It also resembles lichen planus because of the bluish-red color. These lesions are most frequently the very small pinpoint to pinhead-sized lichen syphiliticus and the larger papulosquamous syphilis. Although all groups of these lesions resemble each other clinically, serologic tests, trichophytin, tuberculin, and even luetin tests are positive in their respective conditions. Even with these biologic aids the clinical picture at times is indefinite. Histologic studies, however, show the characteristic picture. The bacterid and trichophytid are acute suppurative processes involving the superficial papillary cutis and overlying epidermis with an infiltrate predominantly of polymorphonuclear leucocytes. The tuberculid, lichen scrofulosorum, involves the same area and consists histologically of epithelioid cells, giant cells, plasma cells and lymphocytes. In addition to the tuberculoid infiltrate, the papulonecrotic tuberculid also shows caseation necrosis of the superficial cutis and epidermis. Lichen scofulosorum and syphilis may be indistinguishable from each other histologically, since they both contain similar minute tuberculoid infiltrates in the papillary bodies of the cutis.

Lichenoid eruptions due to drugs are characterized by a papulosquamous eruption varying in color from bright to bluish red. Depending on the host's reaction, the lesions may be papular, bullous, or urticarial. These eruptions are characterized by severe pruritus, acute onset, and a history of recent medication. Discontinuation of the drug leads to clinical improvement. The most frequent drugs involved are quinacrine, arsenic, acridine, penicillin, and barbiturates.[24]

The histologic structure of drug eruptions varies with the clinical picture. They all are similar in that they involve the upper cutis and the lower rete. Subepidermal as well as intraepidermal vesicles can occur. The cellular infiltrate in the upper

cutis consists of polymorphonuclear leucocytes, lymphocytes, and a number of eosinophiles. The epidermocutis junction is obliterated both by the infiltrate and by localized focal areas of colliquative or liquefaction necrosis of the basal cells of the epidermis. As a result, melanin leaves the basal cells and is found phagocytozed in the histiocytes adjacent to the vessels below the involved epidermal areas. The endothelium of the blood vessels is thicker and there is intrusion of the endothelial cell nuclei into the lumen of the vessel. The lower cutis and the subcutaneous fat are uninvolved. The toxic effect on the arterioles and arteries could be the basis for the erythematous character of the lichenoid lesions.

Histologic Structure

	Lichen Planus	Lupus Erythematosus	Drug Eruption
Epidermis			
Hyperkeratosis	+	+	±
Granulosis	+	±	±
Acanthosis	+	—	±
Colliquative degeneration	+	+	±
Epidermal pegs	+	—	±
Cutis			
Infiltrate character	Diffuse	Localized (globular) perivascular	Diffuse & perivascular
Location	Papillary body	Mid cutis	Upper & mid cutis
Cell type	Pmn. neutrophiles, lymphocytes, & melanin-containing histiocytes	Pure lymphocytes	Variable with prominent eosinophiles
Collagen	Eosinophilic degeneration in upper papillary body	Basophilic degeneration	Unaltered
Elastic fibers	Absent in papillary cutis	Present & increased in amounts in papillary cutis; absent from areas with cell infiltrate	Unaltered
Adnexae	Unaltered	Atrophic	Unaltered
Vessels			
(*a*) No. capillaries	Increased	Unaltered	Unaltered
(*b*) Lumen	Small	Dilated & congested	Endothelial proliferation

Parapsoriasis *en goutte*, poikiloderma, dermatitis herpetiformis, the papular lesions of early mycosis fungoides, and even myelogenous leukemia can be confused with lichen planus. Recently [24] a patient was observed ‖ who clinically had lichen planus, and histologically the lesion resembled a drug eruption. This patient subsequently developed bullous dermatitis herpetiformis and responded dramatically to sulfapyridine medication. Also seen was a patient with definite diagnosis of myelogenous leukemia ¶ who presented cutaneous manifestations which simulated lichen planus. At first glance the microscopic picture resembled lichen planus. The section, when studied in detail, showed the infiltrate to be more focal and perivascular. It was separated from the epidermis by a normal band of connective tissue and contained myelocytes which gave a positive peroxidase reaction.

‖ Nelson, L.: Case presented before the Los Angeles Dermatological Society, Oct. 13, 1953.

¶ Case presented before Dermatologic Staff Meeting, Los Angeles County General Hospital, Oct. 26, 1953.

The diagnosis of a lichenoid eruption can therefore only be made by the integration of the clinical picture with the histologic examination. The histology of the lesion must be able to furnish not one feature but a combination of points that will eventually lead to the correct diagnosis.

SUMMARY

Although the accompanying table best summarizes the differential diagnosis of lichen planus, chronic discoid lupus erythematosus, and the lichenoid drug eruptions, we should like to emphasize the fact that in lichen planus the dominant features in the differential diagnosis from chronic discoid lupus erythematosus are as follows:

1. The great number of melanin-containing histiocytes in lichen planus.
2. The presence of adnexae.
3. Normal elastic fibers found everywhere except in the zone of infiltrate.
4. The absence of perivascular infiltrate in the lower cutis.

In chronic discoid lupus erythematosus and in the drug eruptions secondary to treatment for discoid lupus erythematosus the outstanding characteristics were as follows:

1. Perivascular infiltrate extends deep into the cutis.
2. Elastic tissue is increased in amount in the middle and deeper cutis.
3. Adnexae are absent.
4. Although colliquative degeneration of the basal cells is observed, the melanin-bearing histiocytes are not prominent in the infiltrate.
5. The epidermocutis junction is more sharply demarcated than in lichen planus.

CONCLUSION

After a review of the literature on lichenoid eruptions, we have attempted to clarify some of the confusing features. We believe that lichen planus is a clinical entity and not a syndrome. Further, a lichenoid eruption is one that begins and ends as a papule, showing no progression. Past cases reported as atypical lichen planus or lichen planus erythematosus were, in all probability, drug eruptions. The diagnosis of lichen planus is made by a combination of clinical and histologic characteristics.

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The photomicrographs were made by Mr. William L. M. Martinsen.

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NEGATIVE KAHN STANDARD AND POSITIVE VDRL SLIDE TESTS FOR SYPHILIS

Clinicoserologic Evaluation of Preselected Patients

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A RETROSPECTIVE study of the clinical diagnosis in a group of patients with negative reactions in the Kahn standard test and positive or weakly positive reactions in the Venereal Disease Research Laboratory (VDRL) slide test has been presented in a previous report from this Laboratory.[1] In order that a broader serologic spectrum might be obtained than would be available from hospi-

TABLE 1.—*Postadmission Test Results Obtained at the Venereal Disease Research Laboratory on 270 Patients Admitted to Alto Medical Center with Reactive VDRL Slide Tests and Nonreactive Kahn Standard Tests*

Tests	Nonreactive		Reactive *		Not Tested
	No.	%	No.	%	
VDRL slide	93	34.4	177	65.6	0
Kahn standard	147	55.3	119	44.7	4
Kolmer cardiolipin	54	21.1	202	78.9	14
TPI	29	10.7	241	89.3	0

* Positive, plus weakly positive or doubtful.

tal records, a progressive study of this patient category was designed to include a complement-fixation procedure and the Treponema pallidum immobilization (TPI) test. The latter test was not performed on all patients in this series, and, in some instances, a reportable result by this procedure was not obtained. This report includes only the 270 patients on whom a valid TPI result was obtained. A report covering the entire group of patients studied will be issued at a later date.

METHODS

In county-wide surveys conducted by the Georgia State Department of Public Health, blood specimens were collected and sent to the State Laboratory where VDRL slide tests were performed. All blood specimens found to have weakly positive or positive reactions in the VDRL slide test were further examined with the Kahn standard test. For the purpose of this study, those persons whose blood specimens produced reactive (positive or weakly positive) results in

From the Venereal Disease Research Laboratory (Dr. Olansky, Director; Mr. Harris, Assistant Director; Dr. Edmundson, Associate Director; Miss Rambo, Statistician).

TABLE 2.—*Comparison of TPI with Other Postadmission Test Results by Current Diagnoses of Patients Having Kahn Test Negative and VDRL Slide Test Reactive Prior to Admission*

	Both Reactive	Both Negative	TPI Test Reactive Other Tests Negative	TPI Test Negative Other Tests Reactive
TPI vs. Kolmer Cardiolipin				
Late latent syphilis	81	1	33	12
Early latent syphilis *	4	1	1	1
Neurosyphilis	4	0	1	1
Congenital syphilis	1	0	0	0
No syphilis	8	0	7	1
Total	98	2	42	15
TPI vs. VDRL Slide				
Late latent syphilis	61	4	58	10
Early latent syphilis *	1	0	5	2
Neurosyphilis	1	0	4	1
Congenital syphilis	0	0	1	0
No syphilis	6	0	12	1
Total	69	4	80	14
TPI vs. Kahn Standard				
Late latent syphilis	12	8	106	6
Early latent syphilis *	1	1	5	1
Neurosyphilis	2	0	3	1
Congenital syphilis	1	0	0	0
No syphilis	4	0	14	1
Total	20	9	128	9

* These patients were diagnosed as having secondary syphilis at the time of previous treatment.

TABLE 3.—*Pertinent Findings on Patients Diagnosed as No Syphilis*

Patient, No.	Age	Kahn Standard Test (Units)	VDRL Slide Test (Dils.)	Kolmer C. F. Test (Units)	TPI Test
1	13	2	Neg.	QNS	Pos.
2	50	Neg.	Neg.	QNS	Pos.
3	58	Neg.	< 1	AC	Neg.
4	40	Neg.	Neg.	8	Pos.
5	48	Neg.	Neg.	3	Pos.
6	40	Neg.	Neg.	2	Dbt.
7	11	Neg.	Neg.	32	Pos.
8	38	Neg.	Neg.	3	Pos.
9	42	Neg.	Neg.	7	Pos.
10	42	Neg.	< 1	8	Pos.
11	47	< 1	Neg.	8	Pos.
12	50	1	< 1	Neg.	Pos.
13*	66	1	< 1	Neg.	Pos.
14	50	Neg.	< 1	Neg.	Dbt.
15	31	Neg.	Neg.	Neg.	Pos.
16	12	Neg.	Neg.	Neg.	Pos.
17	32	Neg.	Neg.	Neg.	Pos.
18	46	Neg.	< 1	Neg.	Pos.
19	33	< 1	< 1	8	Neg.
Total reactors		5	7	9	17
% reactive		26.3	36.8	56.2	89.5

* This was the only patient having clinical or historical evidence of syphilis. This patient had a penile lesion 30 years earlier, and his wife had a positive S. T. S.

the VDRL slide tests and negative results in the Kahn standard test were encouraged to go to the Alto Medical Center, Alto, Ga., for a clinical evaluation, which included history, physical examination, spinal fluid examination, and other special studies as indicated. On admission, blood was drawn from these patients and sent to the Venereal Disease Research Laboratory,

TABLE 4.—*Pertinent Findings in Patients with Negative TPI and Reaction in One or More Standard Serologic Tests for Syphilis*

Patient, No.	Age	Current Syphilis Diagnoses	Kahn Standard	VDRL Slide	Kolmer Cardiolipin	TPI	Remarks
20	31	Late latent	1	Neg.	1	Neg.	Fixed pupils; treated, 1945
21	25	Late latent	Neg.	Neg.	8	Neg.	Treated, 1948
22	30	Late latent	Neg.	Neg.	1	Neg.	Treated, 1948
23	30	Late latent	Neg.	Neg.	2	Neg.	Treated, 1940
24	32	Late latent	32	4	32	Neg.	Treated, 1940; one child with congenital syphilis
25	32	Late latent	2	2	8	Neg.	Treated, 1947; stroke; 1947 BP 130/95
26	44	Late latent	1	1	8	Neg.	Treated, 1946
27	41	Late latent	Dbt.	1	8	Neg.	Treated, 1936
28	26	Late latent	Neg.	1	16	Neg.	Treated, 1944; one stillbirth
29	43	Late latent	Neg.	1	16	Neg.	Treated, 1929
30	41	Late latent	Neg.	1	2	Neg.	Treated, 1947
31	53	Late latent	Neg.	1	8	Neg.	Treated, 1935 and 1952
32	40	Late latent	1	1	AC	Neg.	Treated, 1944
33	52	Late latent	Neg.	1	Neg.	Neg.	Treated, 1940
34	31	Early latent	1	1	16	Neg.	Treated, secondary syphilis, 1948
35	21	Early latent	Neg.	1	Neg.	Neg.	Treated, secondary syphilis, 1951
36*	46	Neurosyphilis	3	<1	16	Neg.	Treated, 1944; spinal fluid Kahn 4+, 1952
3*	38	No syphilis	Neg.	<1	AC	Neg.	No clinical or historical evidence of syphilis
19*	53	No syphilis	Dbt.	<1	8	Neg.	No clinical or historical evidence of syphilis

* Reported in other tables.

TABLE 5.—*Pertinent Findings on Complicated Cases*

Patient, No.	Age	Current Syphilis Diagnoses	Kahn Standard	VDRL Slide	Kolmer Cardiolipin	TPI	Remarks
36	40	Neurosyphilis *	3	<1	16	Neg.	Treated, 1944, for neurosyphilis
37	21	Congenital	2	Neg.	16	Pos.	Adequate treatment, 1948, three children, all STS Neg.
38	37	Neurosyphilis *	Neg.	Neg.	32	Pos.	Treated, 1950, for neurosyphilis
39	30	Neurosyphilis *	Neg.	Neg.	Dbt.	Pos.	Treated, 1945, for neurosyphilis
40	45	Neurosyphilis *	Neg.	Neg.	1	Pos.	Treated, 1940, for neurosyphilis
41	46	Neurosyphilis *	1	Neg.	8	Pos.	Treated, 1949, for neurosyphilis
42	45	Neurosyphilis *	1	1	Neg.	Pos.	Treated, 1949, for neurosyphilis

* Asymptomatic CNS.

where the Kahn standard, VDRL slide, Kolmer cardiolipin complement-fixation, and TPI tests were performed. Serologic tests also were performed in the laboratory of the Alto Medical Center, which is a branch of the Georgia State Laboratory.

Diagnoses referred to in this report are those of the physicians at the Alto Medical Center and are based on history, clinical findings, and laboratory findings reported by the laboratory

at the Medical Center or the Georgia State Laboratory. Results obtained at the Venereal Disease Research Laboratory were not reported to the Alto Medical Center doctors, so the diagnoses were not influenced by these findings.

The Kahn standard, VDRL slide, and Kolmer cardiolipin tests were performed in accordance with the techniques listed in the "Manual of Serologic Tests for Syphilis," 1949 [2] with serologic reagents prepared and standardized at the Venereal Disease Research Laboratory. Although the results of these tests were reported as designated in each of the techniques, only the terms reactive (positive, weakly positive, or doubtful) or nonreactive (negative) will be used in this presentation.

The TPI test herein referred to was performed by a slight modification [*] of the original Nelson technique,[3] and reported as positive, negative, or doubtful. If the initial TPI test report was doubtful, the test was repeated and the result of the second test, whether negative, positive, or doubtful, was the final report.

RESULTS

The results listed in Table 1 show the number of nonreactive and reactive findings obtained with each of the four serologic tests. In Table 2 these serologic findings are related to diagnoses issued at the Alto Medical Center. Results obtained with each of the four serologic tests for syphilis, with other pertinent data, from the 19 patients receiving negative diagnosis for syphilis are recorded in Table 3. Table 4 contains the diagnoses, serologic findings, and other data on the 19 patients having negative TPI tests and reactive (positive or doubtful) findings in one or more of the other serologic tests for syphilis. Information obtained about the seven patients having neurosyphilis or congenital syphilis diagnoses is separately presented in Table 5.

COMMENT

Table 1 shows that results obtained in the Venereal Disease Research Laboratory on postadmission blood specimens were at variance with those previously reported by the Georgia State Laboratories on many patients in the 270 selected for this study. The selection method required that each patient have a negative finding in the Kahn standard test but 119 (44.7%) of the 266 blood samples subsequently tested at the Venereal Disease Research Laboratory gave positive or doubtful findings with this test. Although the VDRL slide test initially performed on each of these individuals was reactive, only 177 (65.6%) of the persons tested at the Venereal Disease Research Laboratory gave reactive results in the VDRL slide test. Since one or several weeks may have elapsed between the initial blood test and the time that the patient was admitted to the Alto Medical Center, it is possible that some of the differences noted in laboratory test reports could have been associated with changes that occurred in vivo. However, the proportional differences between the results obtained in the two laboratories is large enough to indicate that the two tests in question were not being performed at the same level of reactivity in both laboratories. Other information at hand also indicates that the Kahn standard test as performed at the Georgia State Laboratories is set at a less reactive level than the same test in the Venereal Disease Research Laboratory.

Figures shown in Table 1 indicate that the VDRL slide and Kolmer tests were appreciably more reactive than the Kahn standard test in this series. It should be be remembered that the method of preselection would establish this test relationship and that these figures would not necessarily be reflective of any serologically

[*] References 3 and 4.

unselected group. The TPI test was reactive in a much higher proportion of the specimens tested than were any of the other three serologic tests for syphilis. This finding probably is a reflection of the proportionately large amount of syphilis, past and present, in this group of patients, since many of them received diagnoses of late latent syphilis and most of the patients had been adequately treated for syphilis some years previously. The consensus among people working with the TPI test is that once TPI antibody is well established in an individual it usually will persist much longer than the reagin detected by the other types of serologic tests for syphilis. Most of the patients in this series who were considered to have had adequate treatment for syphilis were treated during the latent phase of the disease, for the TPI antibody would be expected to persist in these instances.

The relationship of the TPI test to each of the other three serologic tests as presented in Table 2 is similar in that the majority of the disagreements between the TPI and any one of the other tests is in the direction of the TPI being reactive and the other test negative. The other smaller groups in which the TPI is negative and the other serologic test for syphilis is reactive would include the so-called "biologic false-positive" reactors. Even if all of these persons were considered to be false-positive reactors, they would represent a much smaller percentage of the total group than previously had been reported by other investigators.† In this study, only one in each group was considered to be nonsyphilitic.

The 19 persons in this study group who were considered to be nonsyphilitic are listed in Table 3. In this group the TPI test is the most reactive, with a negative report occurring in only two instances. In only one patient of this group (13) is there evidence to support a possible diagnosis of syphilis. This patient had a penile lesion 30 years ago, and his wife has a reactive Kahn and VDRL slide test.

The 19 patients included in Table 4 fit the serologic pattern of the "biologic false-positive" reactors. In each instance the TPI test is nonreactive, whereas reactions were obtained in one or more of the other serologic tests for syphilis. In most of these patients the diagnosis of syphilis was based on documentary evidence of previous treatment by a physician or clinic. However, it may be noted in the remarks in Table 4 that several patients have more than serologic evidence of syphilis. The VDRL slide and Kolmer tests were of approximately equal reactivity in this group, with the Kahn test being less reactive. The method of preselecting this series would force the Kahn test to be in subordinate position in this regard. There is no indication, however, that the negative findings in the TPI test were influenced by the serologic preselection used.

It has been pointed out[5] that treatment during early syphilis may prevent the development of the TPI antibody. This could explain the negative TPI test in Patients 34 and 35 of Table 4, since they were treated in 1948 and 1951, respectively, for dark-field positive secondary syphilis. The TPI findings in Patient 24, who gave birth to a child diagnosed as having congenital syphilis, and 32-year-old Patient 25, who was first treated in 1947 when he had cerebral thrombosis and normal blood pressure, would not fit into the same explanation. The seven patients referred to in Table 5 as having congenital syphilis or neurosyphilis diagnoses in no instance gave positive or doubtful findings in all four of the sero-

† References 6 and 7.

logic tests used. The VDRL test was negative in five of these instances and the Kolmer and TPI tests were each negative only in one. Patient 37 (Table 5), who had congenital syphilis, had positive reactions in all of the tests except the VDRL slide test. This patient, diagnosed as having congenital syphilis which had been treated in 1948, has three children, none of whom have any evidence of syphilis infection. The only patient in this group with a negative TPI test report (36) had weak or strong reactions in each of the other serologic tests. This patient was treated for asymptomatic central nervous system syphilis in 1944, and the Kahn test for spinal fluid still is positive.

The group of patients selected for this study would represent problem diagnoses for the clinician since each of them had discrepant findings (positive and negative) in two serologic tests for syphilis. Findings herein presented emphasize the point that neither the reagin tests using the older lipoidal antigen or the cardiolipin type antigens nor the TPI test may be considered to be diagnostic in terms of present disease. It is apparent that borderline-type serologic reactors may be expected to show the greatest percentage of disagreement between serologic tests for syphilis and that a large proportion of these persons will have positive reactions in the TPI test. Since this latter test may not be positive in the early stages of the disease, and since the positive reaction may be retained for long periods of time after adequate treatment and apparent cure, findings in this test may be less closely related to the present condition of the patient as regards infection with syphilis than are the complement-fixation and flocculation tests for reagin. Serologic tests for syphilis (in whatever combination) must be used in conjunction with all obtainable clinical and historical information about the patient in order that one may come to a rational conclusion in diagnosis.

SUMMARY AND CONCLUSIONS

A large percentage of patients selected on the basis of blood tests showing some reaction in the VDRL slide test and negative findings in the Kahn standard test were found to have syphilis or to have been treated for this disease.

A greater number of positive TPI test findings may be expected in this patient category than would be obtained with complement-fixation or flocculation tests for syphilis reagin.

Positive TPI results may occur in the absence of clinical or historical evidence of syphilis and negative findings with this test may be associated with strong evidence of syphilis infection.

Serologic tests for reagin and the TPI antibody are valuable aids in the detection of syphilis but should not be considered to be, of themselves, diagnostic of the presence or absence of syphilis infection.

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DERMATOLOGIC PROBLEMS IN THE RAILROAD INDUSTRY RESULTING FROM CONVERSION TO DIESEL POWER

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SCHWARTZ [1] stated in a recently published paper, "Prior to the advent of the Diesel type of locomotive there was only an occasional case of occupational dermatitis reported among workers in railroad machine shops and roundhouses. But as railroads began to use Diesels the number of cases of occupational dermatitis increased, so that now it has become a problem."

The dermatitides appearing since Dieselization are indeed perplexing, and they present so many peculiar angles and particular features that they seemed worthy of review and summary. These dermatologic problems can be divided into three groups:

1. Those due to procedures used in cleaning and maintaining engine parts
2. Those due to fuel oil itself
3. Those due to chromates used as anticorrosion agents in Diesel radiators

PROBLEMS RESULTING FROM CLEANING AND MAINTAINING ENGINE PARTS

The operations of cleaning and maintaining Diesel engine parts generally are no different from those used in servicing steam engines. Carbon and grease are cleaned off disassembled motor parts by immersing them in large tanks containing a hot, highly alkaline stripper compound. After this they are steamed off with a special steam cleaner solution. Shop workers are familiar with the irritating effects of these alkaline solutions on the skin and carefully avoid being splashed with them. A dermatitis incurred in this way would be in the category of an accident.

In the cleaning of Diesel engines, however, some special circumstances arise. Birmingham,[1] in a survey of the roundhouses of one railroad, described how the airboxes, surrounding Diesel cylinders were cleaned. These spaces accumulate sand, grit, and soot on their walls, which matter could act as an abrasive if it got into the cylinders themselves. Where he inspected, the entire cylinder heads were sprayed with Diesel fuel oil in the cleaning process. The men engaged in this procedure had considerable contact with the oil from the spray mist. This sort of exposure brings up the second group of dermatologic problems.

PROBLEMS TO DIESEL FUEL OIL ITSELF

Diesel fuel oil is a petroleum distillate of a pale yellow color, with a boiling point higher than that of kerosene. Its solvent properties are such that it can defat the skin surface, thus acting as a primary irritant. Additives, to increase the power of the fuel, may also increase these irritant tendencies.

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Furthermore, some persons have the capacity to develop a true contact-type skin sensitivity to Diesel fuel. This is a totally disabling process usually, as far as railroad employment is concerned. We have seen railroad shop workers, many of them highly skilled, with years of seniority accumulated working with steam engines, who, having developed a Diesel oil dermatitis while in intimate contact with the material, could no longer work in railroad shops in any capacity. Attempts to use them in situations where their contacts would be minimized, such as in supervisory or janitorial capacities, would result in prompt recurrence of their dermatitis.

For example, one man, a skilled machinist, became sensitive to fuel oil soon after his railroad was Dieselized. He was transferred to the railroad's coal docks as a common laborer. He remained free of the eruption, but the coal docks were shut down after conversion was complete. He was returned to the shops and employed in such capacities as roundhouse turnstile operator and janitor. In each situation the dermatitis recurred, and he had to terminate his employment with the railroad.

It seems that practically everything in a railroad shop and roundhouse becomes contaminated with Diesel fuel, and avoidance of contact is practically impossible. Furthermore, it is a volatile material, and highly sensitive people could develop a dermatitis on exposure to its fumes.

CHROMATE DERMATITIS

The skin problems resulting from Diesel conversion have been increased to the proportions of a dilemma because of the use of chrome salts as an anti-rust agent in Diesel cooling systems. Chrome dermatitis has been reported as a dermatological occupational hazard in woolen mills,[2] aircraft plants,* airconditioning equipment maintenance,[7] chrome compound manufacturing,[8] and in lithographic industries.[9]

Various reports have given a rather wide difference in incidence of epidermal sensitivity to chromates in workers exposed to them. Figures from 4 to 27% have been quoted. Hall [10] stated that sensitivity can develop after a comparatively long period of exposure to chromates. This has been our experience. Cases have developed months or years after the patient began to work on Diesel engines.

According to Winston and Walsh [11] the chrome salts are used in very low concentration. These authors report in their investigation that sodium bichromate was used in a strength of 0.08% in Diesel radiator fluid. They mentioned the particular hazard of contact as being in workers engaged in filling and draining the radiator systems. Two of our cases have occurred in men accidentally splashed with residual fluid while working on radiator pumps of systems that had been "emptied."

Many of our cases have resulted, however, from more casual and incidental contact, in persons who were in no way concerned with filling, emptying, or otherwise contacting the Diesel cooling systems. We have had to conclude in such cases that a presumed contact dermatitis is due to chromates when patch tests are negative to fuel, lubricating, and cutting oils, but strongly positive to chromate solution in the strength used in engine radiators. Such reactions have been seen in machinists, disassemblers, laborers, and other railroad shop workers whose exposure to radiator fluid is quite remote. Again apparently, minute quantities of the chromate material get widely disseminated on parts, tools, and other equipment in shops.

* References 3 to 5.

The unusual feature of chromate dermatitis is its chronicity and recalcitrance to treatment. An ordinary contact dermatitis subsides within a week or two after removal of the offending material, provided proper local treatment is administered. In our experience, a chromate dermatitis may persist for weeks, even months, after exposure is discontinued. Becker [12] has suggested that this is due to the setting up of a neurodermatitis, but it seems significant that it happens repeatedly with salts of this metal. The chronicity of this dermatitis calls to mind the chronicity of chrome ulcers, and suggests that the prolongation is the result of fixation of the chromate crystals in the skin itself.

Although the process is difficult to treat by usual methods, it usually responds dramatically to cortisone and corticotropin (ACTH). Hydrocortisone (Compound F) ointment in 2.5% strength, also effectively controls the process. Cole [13] reported good results with dimercaprol (BAL) ointment in chrome dermatitis occurring among lithographers.

SUMMARY AND CONCLUSIONS

The complexities of railroad operations posed by conversion to Diesel power have been added to by the appearance of dermatologic problems among shop workers. The most distressing aspect of this is that these problems may involve men with many years of railroad employment behind them. The potential seriousness of a contact dermatitis renders these men unemployable in railroad shops.

The primary irritating effects of hydrocarbon solvents used in railroad shops can be avoided by protective apparel, use of emollient creams, and adequate washing facilities, as recommended by Schwartz.[14] When allergic contact sensitivity to these materials develops in an employee, he must be removed from contact with them.

The problem of chromate dermatitis is of such proportions in the industry that it would seem to call for search for a practical substitute for use in Diesel radiators. The dermatitis can be produced in a sensitive person who works in any capacity in a railroad shop. It is a prolonged, difficult process to treat, and as an occupational disease is costly to employers.

7026 Jenkins Arcade (22).

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ADENOMATOSIS ORIS

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A CONSIDERABLE amount of confusion exists concerning an entity which consists of a hyperplasia of mucous glandular tissue of the mucous membrane of the oral cavity, with or without associated inflammatory changes. In 1870, Volkmann described as "cheilitis glandularis apostematosa" or "myxadenitis labialis" [1] a supposedly specific form of chronic inflammation of the lower lip. This was characterized as a gradual painless swelling of the lower lip, due to enlargement of the mucous glands, which appeared as a large number of uneven, palpable masses. The excretory ducts were dilated and a thick, purulent secretion could be expressed. This clinical picture suggested multiple, abscess-like lesions with a purulent discharge.[1]

Diffuse enlargement of the upper and lower lips of "macrocheilia" due to glandular hyperplasia in the absence of associated inflammatory change has been described in numerous reports,* and Conway reviews 129 cases from the literature.[8] Microscopic examination in these cases revealed normal glandular tissue of the mucus-secreting variety. In certain cases an infectious etiology is suggested by the presence of inflammatory changes and mucous fistulae, but when there is an absence of cheilitis, it is more suggestive of a congenital local alteration of labial mucous glands. There is no evidence of true tumor formation in any of these reported cases of macrocheilia, although the term "adenoma" has been employed.†

Cheilitis glandularis has been considered by some authors as a precancerous condition.‡ Sutton, in describing cheilitis glandularis apostematosa,§ considered it to be a congenital hyperplasia of the mucous glands and ducts of the lips and associated mucous surfaces such as the buccal mucosa and pharyngeal area. Superimposed or secondary inflammatory symptoms of varying degrees were noted. Histologically, the condition was described as a dilation of the ducts of mucous glands with a thickening of the walls, as well as hypertrophic changes in the acini.

Clinically,‖ cheilitis glandularis is usually described as a condition of enlarged, palpable glands of the oral mucous membrane, with numerous sieve-like openings.

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* References 2 to 7.

† References 5 and 6.

‡ References 9 and 10.

§ References 11 and 12.

‖ References 13 to 18.

Secretion exudes from the dilated ducts and may cause a crusting on the labial mucosal surface. Recently a psychosomatic etiology has been suggested for cheilitis glandularis.[19] In several cases studied there was the typical dilatation of mucous gland ducts and a diffuse lymphocytic infiltrate in the submucosa, but no evidence of hyperplasia of the mucous glands of the buccal mucosa or lips. The possibility of an emotional basis of the syndrome is suggested by demonstrable relationships of many forms of cutaneous disease to psychosomatic factors.[20] Cheilitis glandularis is currently treated by radiation, surgery, or electrocoagulation, but the therapy is generally unsatisfactory.[19]

From this conflicting series of reports it is well to distinguish a relatively rare condition of true hyperplasia of the mucous glands of the lips and buccal mucosa, probably congenital in origin, and unassociated with inflammatory changes or increased glandular activity with ductal dilatation. The oral mucosa, particularly of the lips, is abundantly supplied with mucous glands which can be palpated immediately beneath the epithelial surface when the tongue is pressed against them. The mucous glands are normally about 1 mm. in diameter, and are more numerous in the lower than in the upper lip.[21] The labial glands frequently become cystic (Fig. 5), the lower lip being affected more often. Rarely are they affected to the extent that a pathologic process is suggested.

Our observations on several hundred clinic patients indicate that varying degrees of glandular enlargement exist normally, the labial glands often being palpable and appearing as visible raised papular areas when the lower lip is forced outwards to stretch the mucous membrane. However, cases of extreme prominence of the labial glands are rare. In a study of 4,700 consecutive cases of oral lesions, McCarthy and McCarthy ¶ do not report a single case of extreme hyperplasia of oral mucous glands, although a number of cases of cheilitis glandularis are mentioned. These latter consisted of varying degrees of inflammatory change without marked glandular enlargement. The name "adenomatosis oris" is tentatively suggested as a descriptive term for this condition of extreme hyperplasia of mucous glands of the oral cavity.

REPORT OF A CASE

Mrs. L., a 44-year-old housewife, was referred to the oral medicine clinic by her dentist because of multiple firm papular lesions of the mucosa in the buccal and vestibular areas of the oral cavity. The exact duration is not clear, but the patient states that she has noticed the papular-like nodules for several years and has developed a habit of rubbing her tongue against the involved areas.

Physical examination revealed multiple submucosal firm papular lesions in the buccal mucosa most heavily concentrated at the line of occlusion. The lesions were bilateral. The vestibule of the lips was also involved and by everting the lower lip the nodules became more prominent (Fig. 1). No ductile orifices were observed and no secretion could be expressed after exertion of firm pressure upon the nodules. The lesions were not painful, and there were no unusual subjective symptoms except when the patient pressed her tongue along the involved mucous membrane.

The clinical impression was that these lesions represented mucous glandular elements. One of the papules was excised and the following is the pathologic report.

Pathological Examination.—Under low power, microscopic study of the sections reveals normal mucous membrane, consisting of stratified squamous epithelium overlying fibrous connective

¶ References 24 and 25.

Fig. 1.—Lower lip in a case of adenomatosis oris. The lip is everted to accentuate the numerous nodular masses on the mucosal surface.

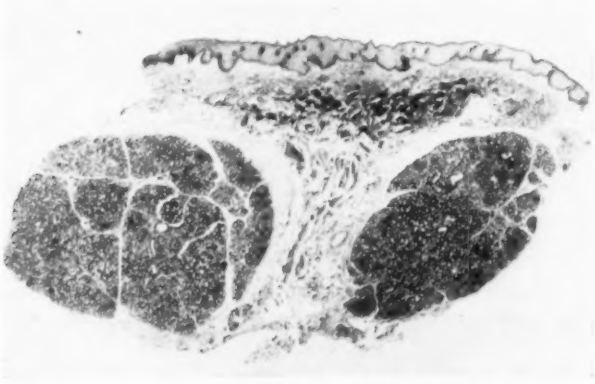

Fig. 2.—Biopsy specimen from raised papular lesion on mucosa of lower lip. Two comparatively large areas of glandular tissue are noted (× 60; hematoxylin and eosin).

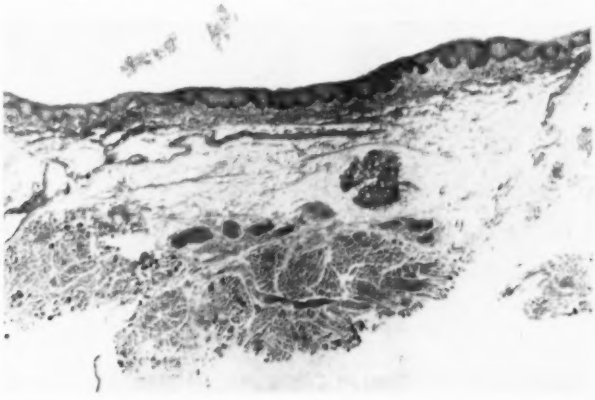

Fig. 3.—Biopsy specimen from mucosa of normal-appearing lower lip. This biopsy was taken in approximately the same area as in Figure 2, for purposes of comparison. Only one small mass of glandular tissue is noted in the loose submucosal tissue. Beneath this the normal musculature of the lip is seen (× 60; hematoxylin and eosin).

tissue. Deep within the connective tissue several large, discrete, circumscribed masses are in evidence (Fig. 2). Upon higher magnification these masses are seen to be composed of mucous glandular elements. The mucous type acini are regular in size and shape, and do not appear distended with mucous secretion (Fig. 4). The glandular tissue appears normal except for a marked increase in amount. There is no infiltration of inflammatory cells, either in the connective tissue or the interacinar spaces of the mucous glandular tissue. No ducts or orifices are noted.

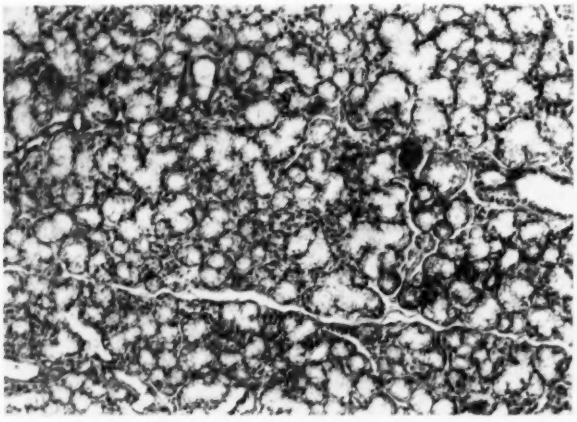

Fig. 4.—Higher power magnification of area from Figure 2. The glandular tissue is of the mucus-secreting variety. There is no notable acinar or ductal dilatation, and infiltration of inflammatory cells is minimal (× 240; hematoxylin and eosin).

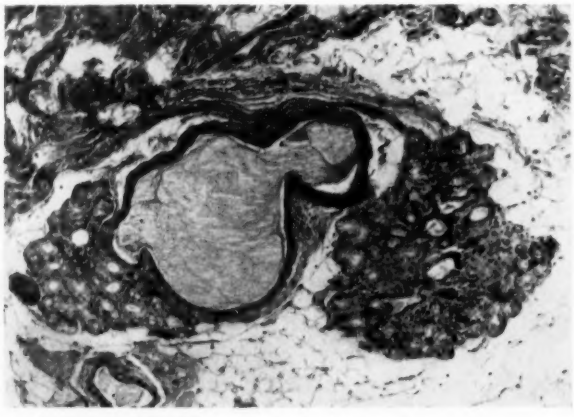

Fig. 5.—High-power magnification of biopsy specimen from normal lip, showing ductal dilatation and cyst formation (× 240; hematoxylin and eosin).

Pathologic Report: Normal mucous membrane with hyperplasia of submucosal glandular tissue.

SUMMARY

A case of extreme hyperplasia of labial and buccal mucous glands is presented. "Adenomatosis oris" is suggested as a descriptive term for this rare entity.

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STUDY OF THE TPI TEST IN CLINICAL SYPHILIS

I. Untreated Early Symptomatic Syphilis

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IT PREVIOUSLY has been reported * that the Treponema pallidum immobilization (TPI) test may be nonreactive during the primary and secondary stages of syphilis. The lipid antigen serologic tests for syphilis, e. g., Kahn, Kolmer, VDRL slide, Rein-Bossak, also may be negative in the presence of dark-field-positive lesions of primary syphilis, but are invariably reactive during the secondary stage of syphilis.[1]

This study of previously untreated dark-field-positive primary and secondary syphilis patients was undertaken to compare the sensitivity of the TPI test, as modified by Portnoy, Harris, and Olansky,[2] in these stages of syphilis with that of the VDRL slide flocculation quantitative and Rein-Bossak slide flocculation quantitative tests.

CLINICAL MATERIAL

Thirty patients with dark-field-positive primary syphilis and 20 patients with dark-field-positive secondary syphilis, who had no history of previous treatment for syphilis at any time, were studied. These were patients either of the Atlanta-Fulton County venereal disease clinic at Atlanta, Ga., or the venereal disease clinic of the City of Monterrey Health Department, Monterrey, N. L., Mexico. Blood was collected from the selected patients and was mailed to the Venereal Disease Research Laboratory at Chamblee, Ga., in the sterile B-D vacutainers.†

LABORATORY METHODS

The serologic tests for syphilis (STS), i. e. the VDRL slide flocculation test quantitative and the Rein-Bossak slide flocculation test quantitative, were performed as described in the Manual of Serologic Tests for Syphilis.[6] Results were termed reactive if the reaction was of any degree, i. e., in less than one dilution or more in either test.

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* References 1 to 3.

† Supplied by Becton-Dickinson Company, Rutherford, N. J. (tube type S3204)

The TPI test was performed with the Nelson and Mayer technique [7] as modified by Portnoy, Harris, and Olansky.[5] Doubtful or positive results in this test were termed reactive.

RESULTS

In Table 1, the 30 patients having primary syphilis are listed with the results obtained with the VDRL slide, Rein-Bossak slide, and TPI tests. All patients who were seronegative in the STS were also negative with the TPI test with the exception of one. This 42-year-old Mexican man may have withheld a history of previous syphilitic infection. It has been reported that the TPI test may remain positive,

TABLE 1.—*Serologic Results in Thirty Patients with Primary Syphilis*

Case No.	Age	Sex	VDRL Dil.	R B Dil.	TPI*	Duration† (Days) Lesions
1	19	M	..	..	N, N	2
2	23	M	..	..	N, N	7
3	18	M	..	..	N	15
4	16	M	..	..	N, N	18
5	26	M	..	..	N, N	20
6	20	M	..	..	N	28
7	27	M	..	..	N	35
8	32	F	..	..	N, N	..
9	21	M	..	..	N	..
10	27	M	..	..	N, N	21
11	23	M	..	..	N, N	42
12	18	M	..	..	N, N	..
13	15	F	..	..	N, N	..
14	25	M	..	..	N, N, P, N	..
15	42	M	..	..	P, P	15
16	18	M	..	1	N, N	20
17	23	M	<1	<1	N, N	20
18	30	M	1	2	P, P	20
19	31	M	1	1	P, P	15
20	19	M	2	2	D, N, N	4
21	31	M	4	8	P, P	21
22	18	M	8	4	N, D, N	..
23	18	M	8	16	P	30
24	27	M	16	64	P, P	10
25	18	M	32	32	N	21
26	47	M	32	64	P, P	14
27	21	F	32	128	P, P	7
28	22	M	32	64	P, P	30
29	17	M	64	128	D	21
30	19	F	128	256	P	21

* P = positive; D, doubtful; N, negative; each test result reported.
† By history (if blank, not known).

and the STS remain negative, after treatment for syphilis,[4] and that a new infection may occur in the presence of a positive TPI test.[5]

In the 15 primary syphilis patients who were seroreactive in the STS, 10 were reactive in the TPI (9 positive, 1 doubtful), interpreting repeated test results according to Nelson's criteria.[9]

The duration of lesions as obtained by history in 19 TPI negative primary patients ranged from 2 to 42 days; the duration of the lesions in 11 TPI reactive patients ranged from 7 to 30 days; other durations were unknown. Many of these histories are considered unreliable on the basis of negative STS findings though the lesion was said to have been present for a considerable period of time.

In Table 2 the 20 patients having secondary syphilis who had no history of previous syphilis infection and or treatment are listed, together with the STS and TPI results obtained. All patients were reactive in the VDRL slide, Rein-Bossak, and TPI tests. Of the TPI results in those 20 patients, 18 were positive, two were doubtful. The durations of the secondary lesions (by history) in eight patients ranged from 4 to 30 days, other durations were unknown. Reliability of duration of signs by history again is considered unreliable.

SUMMARY AND CONCLUSIONS

In 15 patients, who had no history of previous antisyphilitic treatment, with dark-field-positive primary lesions of syphilis, seronegative in the VDRL slide flocculation and Rein-Bossak slide flocculation quantitative tests, 14 were found to be seronegative with TPI tests; 1 patient was found to show a reactive TPI test.

TABLE 2.—*Serologic Results in Twenty Patients with Secondary Syphilis*

Case No.	Age	Sex	VDRL Dil.	R-B Dil.	TPI*	Duration† (Days) Lesions
1	30	M	4	8	P, P	..
2	19	F	8	32	P, P	..
3	13	F	8	16	D, N, D	..
4	32	M	16	32	P, P	..
5	19	M	16	32	P, P	14
6	28	F	16	32	P, P	4
7	25	F	16	64	P, P	..
8	22	M	16	64	P, P	..
9	24	M	32	64	P, P	30
10	15	M	32	128	P, P	..
11	28	F	32	64	P, P	..
12	24	F	32	64	P, P	..
13	16	F	32	32	D, N, D	..
14	16	F	32	128	P, P	21
15	17	F	32	64	P, P	14
16	15	F	64	128	P, P	7
17	20	F	64	128	P, P	..
18	19	M	64	128	P, P	30
19	12	F	128	256	P, P	14
20	37	M	128	....	P	..

* P = positive; D, doubtful; N, negative; each test result reported.
† By history (if blank, not known).

Five of 15 dark-field-positive seropositive (in VDRL slide and Rein-Bossak tests) patients were found negative with the TPI test; 10 were reactive in the TPI.

All of 20 patients who had no history of previous treatment for syphilis, with dark-field-positive seropositive secondary syphilis, were found reactive in the TPI test.

The TPI test is not recommended as a diagnostic procedure during the primary or secondary stages of syphilis. It is evident that this TPI test is not as sensitive in detecting early syphilis infection as the VDRL slide flocculation or Rein-Bossak slide flocculation tests.

Active infectious syphilis may be present in the patient who has reactive or nonreactive STS (VDRL slide or Rein-Bossak) and nonreactive or reactive TPI test results. This should be considered in interpreting TPI test results, and points out the necessity for the physician to relate clinical findings to laboratory test results.

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NOCARDIOSIS OF THE KNEE CAUSED BY NOCARDIA BRASILIENSIS

Report of First Case in a Native of the United States

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ACTINOMYCOSIS or nocardiosis caused by Nocardia (Actinomyces) brasiliensis (Lindenberg, 1909; Castellani and Chalmers, 1913) has been reported chiefly from Brazil and Mexico with possible case reports from other Latin American countries. The organism was isolated for the first time by Lindenberg [1] in Brazil, from a mycetomatous lesion of the thigh, leg, and foot, with resultant limitation in motion of the knee. The name Discomyces brasiliensis was given the organism, and then changed to Nocardia brasiliensis by Castellani and Chalmers in 1913.[2] The first indication of the presence of N. brasiliensis in North America was the report of Boyd and Crutchfield,[3] who described a mycetoma of the foot occurring in a Mexican. They named the organism Actinomyces mexicanus, new species, after comparing it with N. asteroides, which it imitates grossly in culture. Gonzalez Ochoa [4] studied and compared strains of N. brasiliensis, N. mexicana, and N. asteroides biochemically and culturally and found N. brasiliensis and N. mexicana to be identical but distinct from N. asteroides.

N. brasiliensis has numerous strains which cause a variety of clinical lesions. A review by Lacaz [5] of 25 cases of actinomycosis due to N. brasiliensis showed that nine were mycetomas of the leg and/or foot, 4 were generalized cases, 3 involved the knee, 3 the chest, 3 the hand, 1 the shoulder, 1 the neck, and 1 the eye. Yazbek [6] reported eight patients of Lindenberg with lesions caused by N. brasiliensis and illustrated seven of these. All of the lesions were mycetomas of the leg and/or foot, with knee involvement in three of the seven illustrated. Gonzalez Ochoa [7] has also reported a number of mycetomatous lesions caused by N. brasiliensis.

The case reported here is being presented as a primary cutaneous actinomycosis of the knee caused by N. brasiliensis. It represents, as far as we have been able to determine, the first in a native of the United States caused by this actinomycete and indicates that the organism may be more prevalent and widespread than its name would imply.

Studies, observations, and reports from the Dermatological Department of the Barnard Free Skin and Cancer Hospital and the Department of Medicine, Division of Dermatology, School of Medicine, Washington University (Drs. Moore and Lane), and from the Welborn Memorial Baptist Hospital, St. Mary's Hospital, and the Protestant Deaconess Hospital, Evansville (Dr. Gaul).

REPORT OF CASE

G. Q., a 49-year-old white man, an executive, was first observed in September, 1950, with a lesion of the left knee of six weeks' duration. The history of the onset of the lesion was indefinite, although he recalled bumping the knee on the sharp corner of a metal desk. At the time he was remodeling a room and was exposed to old plaster which contained animal hair. The patient stated that the lesion could have resulted from an insect bite.

The family history was noncontributory, except that his mother had died at the age of 35 from tuberculosis.

The patient was raised on a farm and as a boy remembered helping his father treat cattle for "lumpy jaw." He had had the usual childhood diseases. Nothing else in his history was contributory.

When originally observed the raised lesion measured 2 cm. in diameter, was coin-shaped, blue in color, and consisted of numerous closely packed, deep-seated nodules. The remainder of the skin was normal in appearance.

Pus from one of the lesions when examined in potassium hydroxide revealed clumps of tangled mycelium, but a culture was negative. Biopsy material was sent to three different

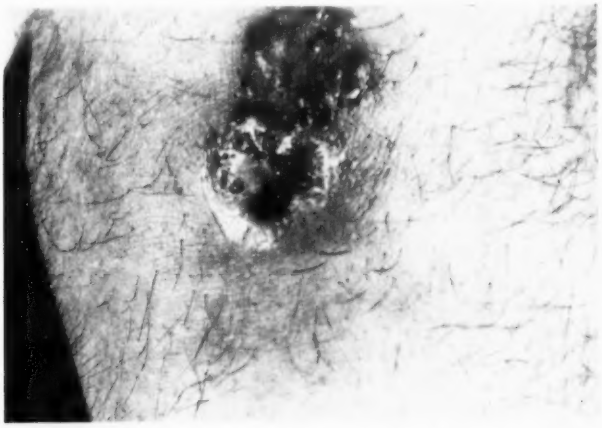

Fig. 1.—Nodular and necrotic lesions of outer aspect of left knee.

dermatopathologists, who made no definite diagnosis, although two suggested the possibility of actinomycosis. One of these two further suggested the possibility of botryomycosis.

On Sept. 10, 1950, the lesion received a total of 2,100 r of unfiltered x-rays. No change in the lesions was noticed from this therapy. On Oct. 23, the lesions were unimproved and there had appeared, 2 cm. above the proximal periphery of the nodules, a glass-like, pin-head-sized, deep purplish nodule. Additional x-ray treatment was given in a dosage of 3,000 r employing the same factors previously used. This dosage produced an intense reaction with only slight regression of the lesion. On Jan. 2, 1951, another biopsy was performed, and complete blood studies were normal. Serologic tests for syphilis were negative. The patient was given chlortetracycline (Aureomycin), 250 mg., four times a day for 10 days, but at no time did this therapy produce any change in the lesion. During the next six weeks the lesion remained stationary, and on May 28, 1951, the patient was referred to St. Louis for consultation.

When observed at this time, the involved area measured 2.5 by 3.5 cm. (Fig. 1). The lower portion of the lesion was composed of several raised, slightly indurated nodules with scaly surfaces. Some of these had hemorrhagic centers. The upper half consisted of about 14 subcutaneous papules, the size of a split pea, with yellowish centers. The clinical impression was

of a mycotic granuloma. The patient was referred for mycologic study. Examination of the tissue revealed a fine-branching, non-acid-fast organism occurring as filaments and coccoid bodies in the form of granules. This suggested the diagnosis of nocardiosis, which was confirmed by culture and smears.

In June, 1951, the entire area was excised, and there has been no evidence of recurrence since that time. Chest x-rays remain normal.

Pathology.—Grossly, the excised tissue consisted of a specimen of skin with subcutaneous tissue measuring 4 by 6 cm. The center of the specimen showed a raised, smooth area measuring 1.5 cm. in diameter, with ulceration. There was a similar and less marked adjacent area. The underlying tissue showed yellowish-red areas.

Microscopically, the epidermis appeared intact (Fig. 2*A*). It was thin in some areas, especially where it was found overlying areas of intense reaction in the dermis. In general, however, the epidermis appeared thickened and showed definite acanthosis.

Throughout the cutis and extending into the fat areas, there was a tremendous cellular reaction which was acutely inflammatory with numerous dilated vessels. The infiltrate was composed of small round cells, wandering connective tissue cells, and macrophages, some filled with blood pigment. These cells were distributed in multiple foci, with a scattering of giant cells of the Langhans type surrounding areas of reaction. Between these areas of reactivity there was a diffuse infiltration of fibroblasts, showing fibrosis. The abscesses were not limited to the cutis but were also found in the epithelial extensions (Fig. 2*B*).

In the center of these abscesses were seen masses of basophilic mycelial elements consisting of filaments and coccoid bodies, the masses appearing either as small spherical groups, reniform or irregular in shape (Fig. 2*C* and *D*). Extending around the periphery of these organisms was a pink-staining substance not in definite club formation. The mycelium was non-acid-fast, although the surrounding substance did have a tendency to be acid-fast (Fig. 2*E*). The organisms were Gram-positive and stained well with methylene blue and eosin.

The whole picture was that of multiple abscesses surrounded by a thin irregular zone of epithelioid cells and giant cells. The abscesses showed evidence of becoming walled off by fibroblasts. In the outlying areas was seen early granulation tissue. The combined observations led to a diagnosis of actinomycosis or nocardiosis.

Mycology.—Small, yellowish-white clumps of intertwined filaments were first seen in material taken from unruptured nodules. These were suggestive of an actinomycete. Cultures were made on Sabouraud's glucose agar with the bloody material taken from the nodules and kept at room temperature. On the fifth day, growth became evident in the form of minute colonies (Fig. 3*A*). These colonies grew slowly and eventually became conglomerate so that on the 22d day they were seen as small discrete to confluent colonies, creamy-white in color, measuring approximately 2 mm. in diameter. On closer examination it was noted that the growth was ochraceous-orange in color and covered with short, aerial, creamy-white mycelium. Stained smears made from the original isolates revealed that the organism was non-acid-fast. In tissue the organism was also non-acid-fast and the gloea-like substance surrounding the mycelial growth was somewhat acid-fast.

Subcultures were made on various media for further study. The appearance of the subcultures, on the media employed, was essentially similar in all cases, with only slight variation in intensity of color or amount of creamy-white aerial mycelium. The colonies became vermiculate to cerebriform, ochraceous-orange in color, with a creamy-white surface growth.

On Sabouraud's glucose agar growth was slow, attaining a diameter of 1 cm. after 19 days (Fig. 3*B*). Individual colonies, after 35 days, appeared mammilliform to crateriform, measuring approximately 2 to 3 mm. in diameter (Fig. 3*I*). The addition of 1% yeast extract to Sabouraud's glucose agar hastened growth somewhat, and the colony measured 1.5 cm. in diameter after 22 days (Fig. 3*C*). The underlying medium developed a brownish discoloration, and the agar showed splitting. On potato-dextrose agar the colony measured 1.5 cm. in diameter after 28 days (Fig. 3*D*), and the color was dull. The underlying medium showed a diffusible

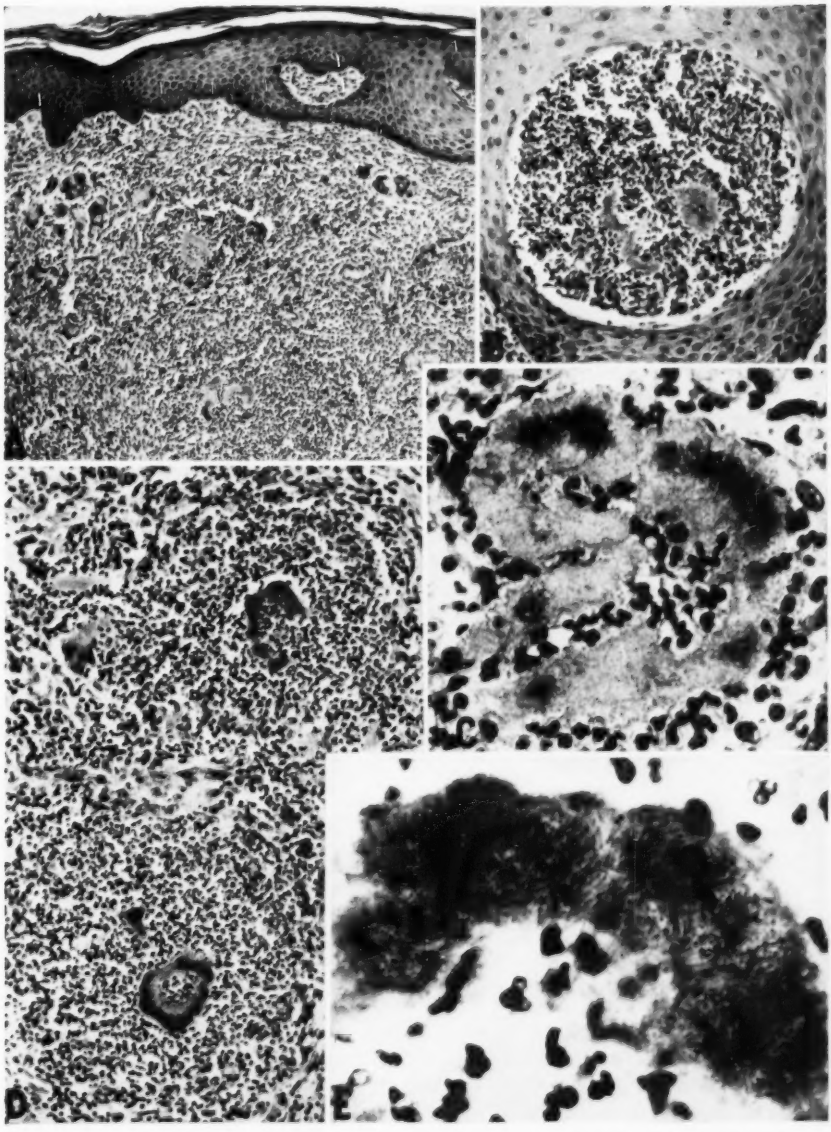

Fig. 2.—*A*, section of lesion showing granulomatous response in cutis with granules (hematoxylin and eosin); × 77. *B*, fungus granules in abscess in epidermal papilla (hematoxylin and eosin); × 127. *C*, granule in cutis showing soft, mucoid-like substance engulfing organisms (hematoxylin and eosin); × 627. *D*, granules within abscesses in cutis (hematoxylin and eosin); × 140. *E*, granule stained with Ziehl-Neelsen method. Filaments and spores are non-acid-fast; × 1,160.

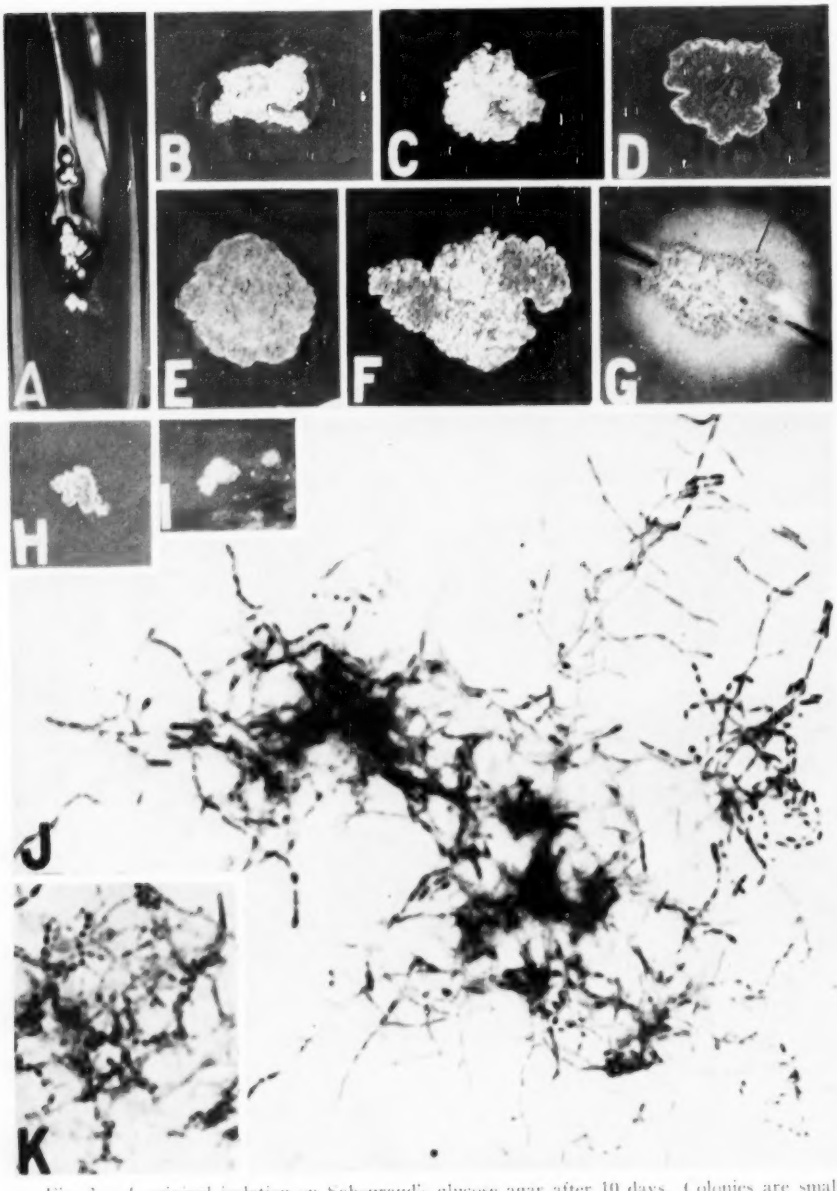

Fig. 3.—*A*, original isolation on Sabouraud's glucose agar after 10 days. Colonies are small and discrete. *B*, subculture on Sabouraud's glucose agar, 19 days old. *C*, subculture on Sabouraud's glucose agar plus 1% yeast extract, 22 days old. *D*, subculture on potato-dextrose agar, 28 days old. *E*, subculture on Sabouraud's glucose agar plus 5% glycerin, grown at 37 C., 22 days old. *F*, subculture on dextrose agar plus 5% glycerin, 35 days old. *G*, subculture on carrot agar, grown at 37 C., 22 days old. *H*, subculture on Czapek's agar, 35 days old. *I*, crateriform colonies on Sabouraud's glucose agar. *J*, floating colony on Long's synthetic medium showing branching filaments and early formation of spores, 22 days old; × 1,720. *K*, same as *J*, showing portion of different colony with spore formation, 22 days old; × 1,720.

brown pigment. On beef extract agar growth was similar to that on potato-dextrose agar. Blood agar subcultures were similar in appearance to those on beef extract agar. A zone of hemolysis surrounded the colony. No swollen cells were seen in smears.

The addition of 5% glycerin to Sabouraud's glucose agar enhanced the growth, with the colony measuring 1.5 cm. in diameter after 22 days (Fig. 3*E*). Growth on this medium was equally good at 37 C. Dextrose agar plus 5% glycerin appeared to be the best medium. The colony measured 1.7 cm. in diameter after 22 days. An irregular periphery was formed and this became more pronounced as the growth increased in size (Fig. 3*F*). The agar showed splitting after 35 days, and the medium showed the diffusible brown pigment.

On carrot agar the colony measured approximately 1 cm. in diameter after 22 days. At 37 C. a grayish opacity developed in the area immediately surrounding the growth. The substratum showed the brown pigmentation (Fig. 3*G*). Growth was good also on carrot and potato plugs. On glycerinated plugs there developed a creamy-white surface growth which was absent when glycerin was omitted.

Growth was poor on Czapek's medium. The colony was yellow in color and measured approximately 0.5 cm. in diameter after 35 days (Fig. 3*H*).

In glucose-peptone broth growth developed as a pellicle on the surface, which was wrinkled and ochraceous-orange in color. A sediment was present on the bottom of the flask, and the broth in between was clear. In Long's synthetic medium plus 5% glycerin growth was poor, forming on the surface small, discrete to confluent, grayish colonies less than 1 mm. in diameter.

Serum was not liquefied. Starch was not affected.

In litmus milk the organism developed as a yellowish-orange to ochraceous-orange growth, chiefly on the surface of the liquid, with some growth on the bottom of the tube. There was no coagulation. The milk became blue (alkaline). Microscopic examination of smears stained by the Ziehl-Neelsen method revealed that some of the filaments and coccoid bodies were weakly acid-fast, particularly those growing on the bottom of the tube.

Gelatin liquefied slowly, beginning on approximately the 10th day, on the surface. The gelatin further showed a brownish discoloration.

Paraffin was utilized as a sole source of carbon. Glass rods dipped in paraffin were placed in flasks of broth inoculated with the organism. Czapek's medium without sucrose was used. Small, spherical, opaque colonies, which became yellow, developed on the rod. These colonies, which were discrete at first, became confluent as they enlarged and covered the whole portion of the rod submerged in the liquid. No other colonies were visible in the medium.

Phenol was not tolerated.

The cultures gave off a distinct moldy or earthy odor, which was not lost on repeated subcultures.

The organism grew equally well at room temperature and at 37 C. when isolated but then grew better at room temperature. It was aerobic.

Microscopically, the organism was seen to consist of fine filaments measuring approximately 0.3 to 0.5 μ in diameter (Fig. 3*J*). Some hyphal enlargements were present. The filaments branched freely, some of the branches occurring at right angles. The filaments broke up at first into long elements, which in turn formed ovoid or coccoid bodies, 0.5 to 1.0 μ in diameter, connected by a clear, lightly staining isthmus (Fig. 3*K*). Some of the terminal bodies were club-shaped, short or elongate, while others were spherical or coccoid. The coccoid bodies eventually became free, increased in size to approximately 1 to 2 μ and were seen in clumps. Filaments and coccoid bodies were seen in the granules in tissue.

The identification of the organism presented a problem when first isolated. Grossly, it had the characteristics of Nocardia asteroides, being verrucous, vermiform, or cerebriform, yellow to ochraceous-orange in color, with a white surface growth on some media. In tissue, however, the filaments and coccoid bodies were not acid fast as is characteristic of N. asteroides. A comparison of the cultural, biologic, and biochemical properties of this organism with other pathogenic, aerobic actinomycetes disclosed a similarity, in most respects, to N. brasiliensis and its synonym, N. mexicana.

COMMENT

The taxonomic status of Nocardia brasiliensis has been subjected to some dispute. When first isolated by Lindenberg in 1909, with subsequent study, it was named Discomyces brasiliensis, new species. Lindenberg described the organism as producing acid-fast filaments in milk. The work of numerous investigators has resulted in the following synonymy for the organism:

Nocardia brasiliensis (Lindenberg, 1909), Castellani and Chalmers: Manual of Tropical Medicine, Ed. 2, 1913, p. 876.

Discomyces brasiliensis Lindenberg, Rev. med. São Paulo, Sept. 20, 1909; Arch. Parasitol. **13**:265-282, 1909.

Streptothrix brasiliensis Greco, Origine des tumeurs, 1916, p. 734.

Actinomyces mexicanus Boyd and Crutchfield, Am. J. Trop. Med. **1**:268-283, 1921.

Actinomyces brasiliensis Gomes, An. paulist. med. e cir. **14**:150-156, 1923.

Oospora brasiliensis Sartory, Champ, Parasit. Homme Anim., 1923, p. 786.

Nocardia mexicanus Ota, Jap. J. Dermat. & Urol. **28**:4, 1928.

The South American investigators, chiefly from Brazil, who have had the opportunity to actually study the organism have agreed with Lindenberg and consider it as a new species. The list includes such workers as Yazbek, Gomes,* and de Almeida and Lacaz.[9] The latter particularly made a comparative study of this organism with Nocardia asteroides in order to definitely establish the validity of the species. The literature has been well summarized by Lacaz.[5] Several other investigators who apparently were not too familiar with the organism itself but rather based their opinion on published descriptions, particularly the property of acid-fastness developed in milk, have considered the organism as N. asteroides. These include Pinoy,[10] Castellani and Chalmers,[11] and Baldacci,* among others.

In 1941, de Almeida and Lacaz carefully set down the characteristics of N. brasiliensis as described by Lindenberg. They further compared the growth characteristics of N. asteroides with N. brasiliensis and concluded that N. brasiliensis was a distinct species. In 1945, Lacaz elaborated considerably on the studies of de Almeida and Lacaz, emphasizing the nature of the soft, yellowish-white granules which occur with or without radiate formation. A detailed study was also presented of the organism, both macro- and microscopically as grown on various media. The biochemical reactions, however, were not considered to be characteristic or constant. In a study of 18 strains of the organism isolated from various lesions, Lacaz found that 9 liquefied gelatin in a varying degree; 9 coagulated and/or peptonized milk; 4 made litmus milk alkaline and 3 made it acid, and 3 reduced nitrates to nitrites.

In Mexico, Gonzalez Ochoa made a comparative study of 3 strains of N. brasiliensis, 5 of N. asteroides, and 10 of N. mexicana. The study included acid-fastness, fragmentation of organism, coagulation of milk, and liquefaction of gelatin. On the basis of this comparative study showing coagulation of milk and liquefaction of gelatin, Gonzalez Ochoa decided that N. brasiliensis and N. mexicana were identical and that the name N. brasiliensis, because of priority, should be retained for the organism. There may be some doubt as to this synonymy, since, as Lacaz has shown, biochemical reaction alone are not dependable as criteria even though Gonzalez Ochoa's work shows an unquestionable similarity in reaction of the strains studied by him.

* References 12 and 13.

The property of acid-fastness has undoubtedly caused some confusion. This characteristic is developed by growing the organism in milk and is not found in other media commonly employed in the laboratory. In this respect it differs greatly from N. asteroides which retains acid-fastness, at least for a while, in the usual media The acid-fastness developed by N. brasiliensis should not be considered as true acid-fastness, as is characteristic of N. asteroides, but merely a pseudophenomenon. In 1886, Bienstock [14] observed that non-acid-fast bacteria could be made acid fast by growing them in lipid-containing media, particularly those containing butter or petrolatum. This work was confirmed by Gottstein.[15] They felt that the fatty substance formed a mantle about the organism and caused it to take the intense stain. Holman,[16] in 1926, found that in lesions in which petrolatum had been used the organisms present might become acid fast. Campbell,[17] in 1925, repeated the work of Bienstock, using a glycerol-broth agar and incorporated butter, hydrous wool fat, or yellow wax in the amount of 1%. After 15 weeks' growth, he found that smears of the various bacteria when washed in ether did not show acid-fastness. Smears not washed in ether, however, did show some acid-fast organisms. These bacteria had a capsule which was probably washed off in the ether treated slides. He concluded that this was not true acid-fastness.

From a clinical standpoint, N. brasiliensis produces chiefly mycetoma involving the extremities and particularly the legs. In some instances other parts of the anatomy have been involved. The knee has been affected on several occasions. Lindenberg in his early publications made note of the frequency of knee lesions, since the first case reported by him and several observed later involved the knee. In 1935, de Almeida [18] reported a case of actinomycosis of the knee with nodular lesions similar to but larger than those in the patient reported here. The organism later identified as N. brasiliensis produced two types of colonies in culture.

SUMMARY

A case of nocardiosis of the knee in a 48-year-old Texan caused by Nocardia brasiliensis is reported with a study of the resultant pathology. This is perhaps the first such case known to occur in a native of the United States.

The cultural and biochemical characteristics of the organism are described. The taxonomy of the organism is discussed; it is considered to be a distinct species and not to be confused with N. asteroides.

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HISTOLOGY OF LUPUS ERYTHEMATOSUS

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GOECKERMAN and Montgomery [1] in 1932 wrote to the effect that the changes in discoid and in disseminated lupus erythematosus are the same and vary only in degree and that a sharp dividing line cannot be drawn. In 1939 Montgomery [2] said that the histologic studies of the skin often permit a definite diagnosis of lupus erythematosus to be established, especially in cases in which the disease is of a disseminated type, but classification as to the type of lupus erythematosus or any conclusion as regards prognosis of a given case cannot be made on the basis of biopsy of a single lesion or groups of lesions.

In 1949 Montgomery and McCreight [3] stated that "we believe that the histologic diagnosis of disseminated lupus erythematosus can be made in the majority of cases, if the specimens for biopsies are taken from a lesion that has not been subject to treatment and if it is at least of several weeks' duration."

In 1950 [4] they stated "it is impossible for one to distinguish between the various types of lupus erythematosus histologically since the microscopic appearances depend more on the age of the individual lesion than on the type of the disease. An early lesion of chronic discoid lupus erythematosus may have the same histologic appearance as a well-developed lesion from an acute disseminated lupus erythematosus."

In 1953 Montgomery * wrote:

> I have seen diagnostic histologic changes as early as three weeks after appearance of erythematous lesions in acute systemic lupus erythematosus, but it is my impression that it usually takes at least six weeks; if biopsy is performed from a lesion in chronic discoid lupus erythematosus that has not been subject to stimulating preparations, radiotherapy, etc., the histologic picture should be diagnostic in upwards of 95 per cent of the cases. I used to think that on histologic grounds, one could differentiate the chronic discoid type from the acute type, but then one sees all gradations and if the site of biopsy is not carefully chosen, one may obtain early lesions in discoid lupus erythematosus which will look just the same as acute disseminate. I think the article with Dr. McCreight emphasized sufficiently the difference histologically between the chronic and the acute disseminate forms of lupus erythematosus. The epidermal changes and keratotic blocking predominate in the chronic discoid type, together with a definite inflammatory reaction in the cutis, whereas, in the acute disseminate type atrophy of the dermis and dilatation of capillaries and lymphatics in the cutis predominate.

Michelson [5] in 1949 summarized:

> the pathologic changes of chronic lupus erythematosus are characterized chiefly by a variability of the degree of edema, infiltrate and epidermal atrophy. The process takes place in a

Read at the meeting of the American Dermatological Association, Lake Placid, N. Y., June 11, 1953.

* Personal communication to the authors.

fairly orderly manner in about the order mentioned. Although this is fairly diagnostic, one must constantly keep the process as a whole in mind and not base his opinion on too rigid a concept. In some instances, chronic lupus erythematosus may be readily recognized microscopically; in others the pathologic changes may be very hard to identify with the disease. The type and size of the lesion and the particular zone from which the tissue was taken should be known. It would be a mistake to state that the findings are pathognomonic. The microscopic anatomy of the skin in acute disseminated lupus erythematosus is well known. Edema, infiltrate and atrophy are encountered in the skin of chronic discoid lupus erythematosus and in the acute form the process is similar, but, as to be expected, is much more rapid and intense. Edema and necrosis are outstanding features.

Michelson stressed that hemorrhages are associated with the edema and that the infiltrate is not so dense or so plentiful as in the chronic type. He concluded that there is a decided similarity between the cutaneous pathology of the acute disseminated type and the chronic form, the outstanding difference being the intensity of the process in the former.

Lever [6] states that in chronic discoid lupus erythematosus "in most instances a histologic diagnosis is possible on the basis of a combination of pathologic findings. There are five cardinal changes in the skin: (1) hyperkeratosis with keratotic plugging; (2) atrophy of the rete malpighii; (3) liquefaction degeneration of the basal cells; (4) a patchy, perivascular, chiefly lymphocytic infiltrate with a tendency to arrangement about the dermal appendages, and (5) basophilic degeneration of the collagen and of elastic fibers. Not all five changes are present in every case." In the subacute disseminate form "the histologic changes in the lesions differ only in degree from those of chronic discoid lupus erythematosus, whereas the hyperkeratosis and the inflammatory infiltrate are less marked. Thus, the histologic picture assumes a less diagnostic appearance. Nevertheless, the combination of atrophy of the epidermis and marked liquefaction degeneration of the basal layer is strongly suggestive of subacute disseminate lupus erythematosus."

In the acute systemic type the "fundamental lesion is fibrinoid degeneration of the collagen. The histologic appearance of the skin in acute systemic lupus erythematosus resembles that of subacute disseminate lupus erythematosus."

PRESENT HISTOLOGIC STUDIES

We stated [7] in 1951 that the microscopic findings in a well-developed chronic discoid type of lupus erythematosus (Table 1) and from a cutaneous lesion of the acute systemic type were rather diagnostic. On the basis of a study of 213 cases we concluded that it frequently was possible to predict the diagnosis and the type of lupus erythematosus, although prognosis should not be based only on histopathologic grounds.

In a compartive study of 163 cases (Table 2 and Fig. 3) of chronic discoid lupus erythematosus, we found that the average keratin layer was about 55 μ wide. In the 25 sections from clinically subacute cases the keratin layer was essentially the same width, and in 25 sections from the acute type of lupus erythematosus the keratin layer was only slightly less. An important feature was that, although the average width of the keratin layer in chronic discoid was 55 μ, the keratin layer varied from 10 to several hundred microns. About 30 per cent of all forms had a keratin layer of over 50 μ, but hyperkeratosis over 100 μ practically never occurred

in the more acute forms. Some hyperkeratosis may occur in all three stages, and mild hyperkeratosis is not a characteristic finding of any particular stage. Plugging is characteristic of chronic discoid lupus erythematosus but decreases as the erup-

TABLE 1.—*Histologic and Clinical Diagnoses*

Histologic Diagnosis	Clinical Diagnosis	No.	%
Acute lupus erythematosus, 25 cases	Acute	15	60
	Died	9	36
	Subacute	6	24
	Disseminated	2	8
	Total acute or subacute	23	92
	Chronic disseminated	0	0
	Unknown	2	8
Subacute, 25 cases	Acute	3	12
	Died of lupus erythematosus	2	8
	Subacute	4	16
	Disseminated	8	32
	Total acute or subacute	15	60
	Chronic disseminated	5	20
	Chronic discoid	3	12
	Unknown	2	8
Chronic discoid, 163 cases	Unknown	1	0.6
	Acute	1	0.6
	Died	0	0
	Subacute	6	3.7
	Disseminated	4	2.4
	Chronic disseminated	19	11.7
	Chronic discoid	132	81.0
	Total chronic	151	92.7

TABLE 2.—*Histopathologic Findings in Lupus Erythematosus*

CUTIS EPIDERMIS		Chronic Discoid—163 Cases		Subacute—25 Cases		Acute—25 Cases	
		Avg.	46 μ	..	44 μ	..	37 μ
		..	%	..	%	..	%
	Keratin	Above 50 μ	19	..	16	..	12
		Above 100 μ	9.2	..	4	..	None
	Plugging	92	56	11	44	3	12
	Atrophy	129	79	24	96	25	100
	Acanthosis	30	18	None		None	
	Edema	125	76	25	100	25	100
	Crusting or vesicles	None	..	2	8	5	20
	Edema	42	26	14	56	22	88
	Infiltrate						
	1. Sparse	Seldom		13	52	24	96
	2. Superficial	81	50	16	64	17	68
	3. Deep	110	67	6	25	None	
	Blood vessels	1	Avg.	1.2	Avg.	1	Avg.
	Collagen	1.4	Avg.	1.1	Avg.	1	Avg.

tion "becomes more acute," occurring in only about 20% of the acute types. Atrophy of the epidermis, portrayed as loss of rete pegs and decrease in width of the rete, occurred in about 100% in the more acute forms and in approximately 90% in the more chronic forms. Some acanthosis may at times be seen in some areas in a biopsy specimen from the more chronic types.

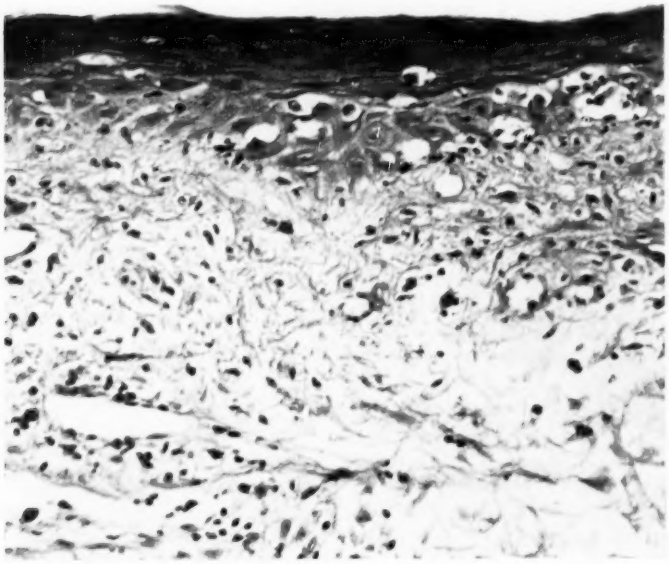

Fig. 1.—High-power photomicrograph from a case of acute lupus erythematosus. Shows atrophy of the epidermis, intracellular edema of the lower epidermal cells, especially the basal cells. These cells are distorted by the intracellular edema and their nuclei have become pyknotic. There are dilated capillaries, moderate edema, and a mild diffuse subacute infiltrate, composed of small monocytes and a few fibrocytes, throughout the cutis.

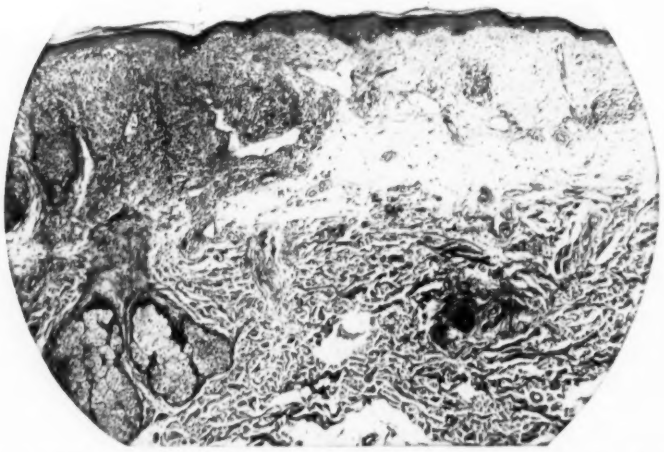

Fig. 2.—Low-power photomicrograph. On the left one sees the characteristic picture of chronic discoid lupus erythematosus. The epidermis is atrophic with some intracellular edema of the basal cells and in the upper and mid cutis a dense well-defined small mononuclear infiltrate. On the right the cells of the basal layer do not show much edema, but the lack of infiltrate and the edema of the upper cutis are suggestive of the acute form. The areas showing the acute changes were several hundred microns wide.

Edema occurs in lupus erythematosus in the epidermis, mainly in the basal layer, and principally as an intracellular edema. The basal cells lose their normal architecture as the disease "becomes more acute." The intracellular edema of the basal layer is more prominent in the acute and subacute forms. The edema appears as an intracellular vacuolation (liquefaction degeneration), replacing the cytoplasm and displacing the nucleus, which becomes pyknotic, so that the basal cells lose their characteristic morphology.

This form of intracellular edema occurs in about 100% in the more acute forms and in about 75% in the chonic discoid type, but it also becomes more advanced

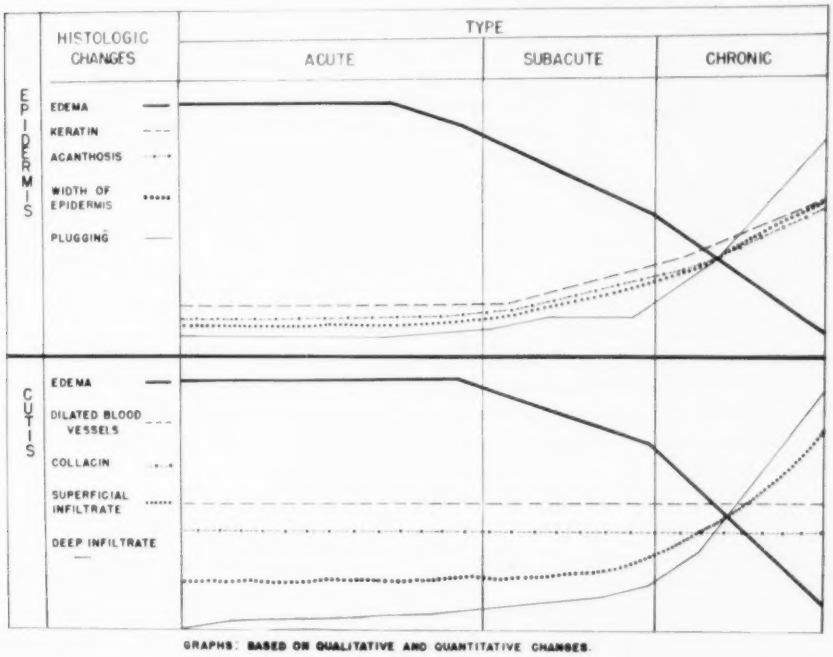

Fig. 3.—Graphs based on qualitative and quantitative changes in lupus erythematosus.

as the eruption becomes more acute. In contrast to Michelson's finding, we found relatively little crusting or necrosis of the epidermis in the acute form of lupus erythematosus; in fact, we think that this usually occurs only in the terminal stages, and, of course, biopsy specimens are usually taken in such a way as to avoid such areas in order to obtain an uncomplicated histologic picture. Vesicles and crusting were lacking in the chronic discoid form but occasionally were found in the acute types.

Edema in the cutis in lupus erythematosus may occur in all types, but it was seen to any extent in only 25% of cases of the chronic discoid form, increasing as the eruption became more acute. It was very extensive in many cases in the acute form.

A well-defined dense perivascular and perifollicular infiltrate is characteristic of chronic discoid lupus erythematosus. The infiltrate consists principally of small monocytes with a few large monocytes. Seldom is there much or a dense superficial or subepidermal infiltrate but more frequently a deeper infiltrate in the midcutis and lower cutis, starting about 100 to 200 μ below the epidermis. A sparse superficial infiltrate may be present in the acute stage, but only when the epidermis becomes so thin or atrophic that it is unable to perform its true function does a secondary infiltrate occur. Also as the process becomes more acute, the deep infiltrate decreases or even disappears. A deep infiltrate occurs so often to the bottom of the section in the discoid type that we see little reason histologically for differentiating chronic discoid lupus erythematosus into a superficial and a deep, or profunda, type.

The number of blood or lymph vessels present and their amount of dilatation are about the same in all types but may have been a little more prominent in the subacute. In regard to basophilic collagen or the alterations toward this final product, these changes are seen in all types but are seen best in the chronic discoid type. We essentially agree with Montgomery that senile elastosis depends more on the site of the biopsy than on the stage of the disease; i. e., in sections from the uncovered areas, the basophilic collagen changes were better developed than in sections from the covered areas. We seldom found any fibrinoid degeneration even in the sections from acute cases.

Present Histologic vs. *Clinical Studies.*—In order to obtain 100 biopsy cards on which the histologic diagnosis of lupus erythematosus was made or clinically suggested, 1,669 consecutive biopsy cards had to be surveyed. Seventy of the biopsy cards were sent in by members of the Board of Dermatology (24 of these by us); 21 by postgraduate students in dermatology; 8 by dermatologists who were nonboard members, and 1 by a nondermatologist. Three biopsies had to be discarded because they were unsatisfactory.

HISTOLOGIC DIAGNOSES

Seventy-five of the cards (Table 3) had a histologic diagnosis of lupus erythematosus, 44 of the chronic discoid type, 21 of the subacute type and 10 of the acute type. Other histologic diagnoses were chronic inflammation, seven; lichen planus, sarcoid and basal cell epithelioma, two each, and one each of the following diagnoses: erythema annulare centrifugum, syphilis, erythema multiforme, toxic vasculitis, abscess, prickle cell epithelioma, neurodermatitis, morphea, lymphoma, reticulum cell lymphoma, lymphocytoma, and senile keratosis.

Out of 44 cases diagnosed histologically as a chronic discoid type of lupus erythematosus, 29 (66%) were so diagnosed clinically. Seven were diagnosed clinically as unspecified lupus erythematosus. If these are combined, the correct clinical diagnosis was suggested in 82%. Actually lupus erythematosus of some form was suggested in 40 of the 44 cases, or 90% of the clinical impressions agreed with histologic diagnosis as far as the disease was concerned.

Other clinical diagnoses made or suggested in those diagnosed histologically as chronic discoid lupus erythematosus were epithelioma, five; tertiary syphilis, three; granuloma annulare, three; sarcoid, two; one each of lymphocytoma, eosinophilic granuloma, insect bite, erythema perstans, erythema annulare centrifugum, actinic dermatitis, lichen planus, lupus vulgaris, papulonecrotic tuberculid, and lichenoid dermatitis.

In subacute lupus erythematosus there were 21 sections so diagnosed; in 8 the chronic discoid type was suggested clinically; in 5 an unspecified type; in 5 the subacute type and in 2 the chronic disseminated type. The clinical diagnosis of lupus erythematosus was suggested in 20 of the 21 biopsies so diagnosed, and the clinical diagnosis was therefore suggested in 95% as far as the disease was concerned. The type agreed in 25%, but chronic disseminated gives practically the same histologic picture as subacute lupus erythematosus, especially if the biopsy is from any area of the body other than the face or neck. Biopsies from the hand, foot, and mucous membrane show changes similar to lichen planus, even in the chronic forms of the disease.

TABLE 3.—*Histologic Compared with Clinical Diagnoses*

Histologic Diagnoses of Lupus Erythematosus	Clinical Diagnoses: Lupus Erythematosus		Clinical Diagnoses: Other	
Chronic discoid, 44, cases	Chronic discoid	29 (66%)	Epithelioma	5
	Unspecified	7	Syphilis	3
	Subacute	2	Granuloma annulare	2
	Acute	1	Sarcoid	2
	Superficial	1	Other	12
	Total	40 (90%)		
Subacute, 21 cases	Chronic discoid	8	Actinic dermatitis	2
	Unspecified	5	Contact dermatitis	3
	Subacute	5	Lupus vulgaris	2
	Chronic disseminated	2	Other	11
	Total	20		
Acute, 10 cases	Chronic discoid	1	Other	3
	Unspecified	2		
	Subacute	3		
	Chronic disseminated	1		
	Acute	3		
	Total	10		

Summary	Hist.	Clin.
Chronic discoid	44	40
Subacute	21	20
Acute	10	10
Total	75	70 (93%)

The following clinical diagnoses were also suggested in the patients diagnosed histologically as having subacute lupus erythematosus; three, contact dermatitis; two, actinic dermatitis and lupus vulgaris; one each, fibrocaseous tuberculosis, erythema annulare centrifugum, erythema multiforme, seborrheic dermatitis, granuloma annulare, rosacea, eczema, tuberculosis cutis, sarcoid, and metastatic carcinoma, and in one case the diagnosis was deferred. Two diagnoses were suggested five times, three diagnoses twice, and five diagnoses twice.

In acute lupus erythematosus there were 10 cases diagnosed histologically as such. The clinical impression in three (30%) of these was acute lupus erythematosus; in three, subacute lupus erythematosus; in one, chronic discoid lupus erythematosus, and in two, lupus erythematosus, type unspecified. Only one was suggested as having a chronic discoid type. In all the biopsies diagnosed acute lupus erythematosus, the clinical diagnoses of lupus erythematosus were suggested.

In the 10 cases that were diagnosed histologically as acute, the following diagnoses were also suggested once: poikilodermatomyositis, actinic dermatitis, and dermatitis medicamentosa. Two diagnoses were suggested three times.

CLINICAL VS. HISTOLOGICAL DIAGNOSES

In one of the 100 biopsies (Table 4) studied, no clinical impression was given but was deferred pending biopsy. In the remaining 99 specimens, 171 clinical impressions had been made. The discrepancy in numbers is due to the fact that in 42 cases

TABLE 4.—*Clinical Compared with Histologic Diagnoses*

Clinical Diagnoses Lupus Erythematosus		Histologic Diagnoses Lupus Erythematosus, Type	
Chronic discoid	47	Chronic discoid	29 (62%)
		Subacute	8
		Acute	1
			38 (80%)
		Other	9
Chronic disseminated	3	Subacute	2
		Acute	1
Subacute	12	Chronic discoid	2
		Subacute	5
		Acute	3
		Chronic inflammation	2
Acute	5	Chronic discoid	1
		Acute	3
		Toxic vasculitis	1
Type unspecified	26	Chronic discoid	7
		Subacute	5
		Acute	2
			14
		Other	12

Summary	Hist.	Clin.
Chronic discoid	47	38
Subacute	12	10
Disseminated	3	3
Acute	5	4
Superficial	2	1
Type unspecified	26	14
Total	95	70 (74%)

more than one clinical impression was given. In 21 cases two clinical impressions were made; in 15, three clinical diagnoses; in 3, four clinical diagnoses; in 3, five clinical impressions and in 57 write-ups only one clinical diagnosis was given.

In 95 of the patients studied, some type of lupus erythematosus was considered in the clinical impression. Of these, 47 were considered clinically to be of the chronic discoid type, 3 of the chronic disseminate type, 12 of the subacute type, 5 of the acute type, 2 of the superficial type, and 26 times the impression of lupus erythematosus was made without signifying the type that was considered.

Of the 47 cases in which chronic discoid lupus erythematosus was considered clinically, 38 (80%) showed the histologic picture of lupus erythematosus; 29 (62%

agreement) of these were considered to be chronic discoid, 8 (17%) subacute and 1 acute. The remaining histologic diagnoses were chronic inflammation, three; basal cell epithelioma, prickle cell epithelioma, sarcoid, senile keratosis, and abscess, one each.

All three of the cases in which the chronic disseminate type was considered clinically showed the histologic picture of lupus erythematosus, two of the subacute and one of the acute type. It is our impression that chronic cutaneous dissemination (not the same as acute systemic) shows essentially the same histologic picture as subacute lupus erythematosus.

The histologic picture of lupus erythematosus was seen in 10 of the 12 biopsy specimens taken from patients suspected of having subacute lupus erythematosus. Two of these were of the chronic discoid type; five, subacute; three, acute. In the remaining two instances the histologic diagnosis was chronic inflammation.

Four of the five patients in whom the impression of acute lupus erythematosus was made showed lupus erythematosus histologically, one of the chronic discoid type and three of the acute type. In the fifth case, the histologic diagnosis was toxic vasculitis.

In the 26 in which the type of lupus erythematosus was not given, only 14 (54%) were histologically diagnosed lupus erythematosus. The less frequent agreement of clinical and histologic diagnoses in this group is probably because in many cases lupus erythematosus was but one of several conditions considered clinically, or, in a few cases, some other clinical diagnosis was considered more likely but a biopsy was performed to "rule out lupus erythematosus." The histologic diagnoses in this group were chronic discoid lupus erythematosus, seven; subacute lupus erythematosus, five; acute lupus erythematosus, two; chronic inflammation, two; lichen planus, two; basal cell epithelioma, sarcoid, erythema multiforme, neurodermatitis, lymphoma, lymphocytoma, reticulum cell lymphoma and erysipelas, one each.

Clinical impressions other than lupus erythematosus were epithelioma, seven; contact dermatitis, seven; sarcoid, seven; granuloma annulare, six; tertiary syphilis, six; actinic dermatitis, five; lichen planus, five; lupus vulgaris, three; seborrheic dermatitis, erythema annulare centrifugum, psoriasis, erythema multiforme, rosacea, tuberculosis cutis, two each; fibrocaseous tuberculid, papulonecrotic tuberculid, rosacea-like tuberculid, urticaria, lymphocytoma, poikilodermatomyositis, eosinophilic granuloma, insect bite, erythema perstans, lichenoid dermatitis, eczematous dermatitis, dermatitis medicamentosa, mycosis fungoides, leucoplakia, seborrheic keratosis, erythema nodosum, periarteritis nodosa and metastatic carcinoma, one each. In one case the clinical diagnosis was deferred.

The majority of the above diagnoses were given as clinical impressions in addition to the clinical impression of lupus erythematosus. Only five instances of histologic lupus erythematosus were encountered in which the clinical impression of lupus erythematosus was not mentioned. In the instance in which the diagnosis was deferred, the histologic picture of subacute lupus erythematosus was seen. There were two cases with a clinical impression of epithelioma which proved to be chronic discoid lupus erythematosus histologically, one thought to be poikilodermatomyositis clinically but acute lupus erythematosus histologically and one in which

three clinical impressions, lymphocytoma, eosinophilic granuloma or insect bite were suspected but which was diagnosed chronic discoid lupus erythematosus histologically.

DIFFERENTIAL DIAGNOSIS

It would make this article too long to give in adequate detail the histologic differential description of the diseases that should be considered in the differential diagnosis, but the more important of these diseases are listed.

Senile elastosis
Actinic dermatitis
Lichen planus
Atrophic lichen planus (lichen plano-pilaris, lichen planus et acuminatus atrophicans)
Poikiloderma atrophicans vasculare
Syphilis—secondary
Erythema annulare centrifugum
Lichen sclerosus et atrophicus
Early scleroderma
Acrodermatitis chronica atrophicans
Erythema multiforme
Lymphoblastomas

COMMENT

From the histologic point of view, there is little doubt that chronic discoid lupus erythematosus, subacute lupus erythematosus and acute lupus erythematosus are one disease: the transition from one "type" or "form" to another can be demonstrated. Occasionally the chronic discoid type shows small areas with a picture suggestive of the acute type. These usually are only in relatively small areas (several hundred microns) and it is therefore necessary to have a large enough biopsy in order adequately to "read" the section. We suggest the biopsy should preferably be not less than 5 mm. in diameter and at least 2 mm. deep. It is our impression that the histology of lupus erythematosus is usually diagnostic, especially in the chronic discoid type, and it is usually possible to differentiate the chronic discoid type from the subacute and acute types of lupus erythematosus. The subacute forms are more difficult to differentiate from the acute type. Clinical cutaneous dissemination, especially if the biopsy is taken from some part other than the head or neck, usually gives the histologic picture of a subacute type of disease, even though clinically the eruption is chronic.

It is our impression that a moderately fixed erythematous eruption on the cheek, that may disappear during the winter and recur during the summer, will show essentially the same histologic picture as chronic discoid lupus erythematosus, although there may be a little more edema and a little less infiltrate.

We were unable to confirm or disprove Montgomery's findings that the early lesion of chronic discoid lupus erythematosus may show the same histologic picture as the more acute forms because of lack of suitable cases.

We have seen sections from patients that suggested acute lupus erythematosus before the clinical findings or diagnosis confirmed the histologic diagnosis. In one patient three biopsies over a period of five years were rather diagnostic of acute

lupus erythematosus before the patient developed the clinical signs, symptoms and laboratory findings, including the lupus erythematosus cells, diagnostic of acute lupus erythematosus.

SUMMARY

The histopathologic picture of lupus erythematosus is rather characteristic. The chronic discoid type can usually be differentiated from the more acute forms. In a rather high percentage of sections from acute lupus erythematosus the diagnosis of acute lupus erythematosus can be made on the histologic findings alone. From the clinical point of view, although in most cases the well-trained dermatologist can usually suspect the diagnosis of lupus erythematosus, nevertheless he should find the histologic examination a valuable aid in confirming this diagnosis and also in suggesting the type or form. We wish in no way to infer that the pathologist's opinion as to the type of disease should be taken with any finality. The dermatohistopathologist, on the other hand, should not be content to make just the diagnosis of lupus erythematosus, but should attempt to suggest the type.

CONCLUSION

1. Chronic discoid and acute lupus erythematosus each usually show a distinct but different histologic picture.

2. The acute form is characterized by marked atrophy of the epidermis with severe edema in the lower cells of the rete. In the cutis the lack of infiltrate and the extreme edema are the characteristic features.

3. The chronic discoid type usually shows more hyperkeratosis and plugging, and less edema in the epidermis and cutis, plus a dense well-defined small mononuclear, frequently periappendageal, infiltrate.

4. The subacute forms usually portray more the characteristic of the acute form with less edema and more infiltrate than the acute type.

ADDENDUM

We were on the lookout for hematoxylin bodies in our histologic sections of lupus erythematosus, but did not find any in our sections.

8 E. Madison St. (2).

840 Park Ave. (1).

ABSTRACT OF DISCUSSION

DR. CLARK W. FINNERUD, Chicago: The authors have well reviewed the known facts with regard to the histologic findings in the various types of lupus erythematosus as expressed by a number of the outstanding authorities. It would be superfluous for me here to reiterate or stress these diagnostic features.

I formerly believed and taught that on histologic grounds alone a definite diagnosis of lupus erythematosus could be made in more than 95% of the cases studied, and that on those grounds a fairly accurate diagnosis as to the type of the disease present could be stated in upward of three-quarters of the instances. As the result of proved errors, I have long since come to the point of greatly modifying those figures, particularly with regard to the type of the disease present, for the well-recognized reasons reviewed in the text of this presentation.

Although there is sufficient evidence to warrant justification for assuming that the localized and systemic types of lupus erythematosus constitute a single disease process, I am convinced that unequivocal differentiation cannot be made histologically between the three types of lupus

erythematosus. No definite criteria having as yet been established, the clinical picture and laboratory findings remain up to the present our only means of conclusively differentiating the chronic discoid and systemic types of the disease.

DR. MICHAEL H. EBERT, Chicago: The general pathologist is not greatly impressed as a rule by our criteria for the diagnosis of discoid lupus erythematosus in histologic sections. He is also anxious to find any pathologic evidence that discoid and systemic lupus erythematosus are closely related diseases. We had a very interesting experience recently at the Presbyterian Hospital of the city of Chicago with a man in his forties who had suffered for a number of years from a well-authenticated chronic discoid lupus erythematosus. He died suddenly of causes entirely unconnected with the lupus erythematosus. On postmortem examination the typical onion type of fibrosis was found about the penicillary arteries of the spleen. This was identical with the type found in most cases of systemic lupus erythematosus.

DR. HERMAN BEERMAN, Philadelphia: We have had the opinion that the histopathology of lupus erythematosus was clear-cut. Dr. Ellis has more or less confirmed that impression. However, I would like to add a note, not in a critical sense, but rather in an elaborative sense, to further the points which he has already so well stated. In the first place, we all agree, I believe, as to the criteria for the diagnosis of lupus erythematosus, be it acute, subacute, or chronic, and that they all may appear in the same specimen if the specimen is adequate, properly taken, and from the proper phase of development of the lesion. There are, however, other phenomena which may produce microscopically a lupus-erythematosus-like picture and yet, perhaps, not be that disease at all or be that disease in a form which is as yet unrecognized as part of the lupus erythematosus syndrome. This is similar to the situation with sarcoidosis. Thus the sarcoid reaction may be produced by many phenomena: beryllium disease, leprosy, and so forth. Likewise, it is possible that there is a lupus-erythematosus-like reaction which also may be produced by adverse factors, e. g., light.

This is anticipated to some extent by a statement made by Dr. Ellis to the effect that "it is our impression that a moderately fixed erythematosus erosion on the cheek may disappear during the winter and return in the summer and will show eventually the same histologic picture as chronic lupus erythematosus, although there may be a little more edema, a little less infiltrate," and subsequently he said that one patient had lupus erythematosus histologically for five years preceding the development of the disease clinically.

This brings up a subject which Drs. Lamb and Shelmire have discussed before this group, and which Drs. Cahn, Levy, Shaffer and I have recently presented before the Society for Investigative Dermatology, namely, that abnormal response to light may imitate histologically the picture of lupus erythematosus in every respect. I think Dr. Lamb, who does not entirely agree with this point, admits that this is true in some cases. Therefore, it is possible that various other factors, in addition to sunlight, such as trauma, may produce the lupus erythematosus microscopic picture. These may represent subclinical or as yet undeveloped lupus erythematosus.

DR. LOUIS H. WINER, Beverly Hills, Calif.: Dr. Ellis has done extensive work in studying so many sections and in analyzing the data obtained from them.

I am occasionally puzzled by histologic sections of chronic discoid lupus erythematosus in attempting to differentiate them from solar dermatitis, fixed drug eruption, and lichen planus. These conditions all have groups of signs in common. However, an occasional individual characteristic separates each member of this group from the other. For example, all of them have liquefaction degeneration of the basal cells, hyperkeratosis, and lymphocytic cellular infiltrate. However, lichen planus is separated by the zonal increase in the stratum granulosum. Lupus erythematosus and solar dermatitis may both have hyperkeratotic plugging, but solar dermatitis most frequently has epithelial necrosis. Both of these conditions can at times stimulate lymphoma to a high degree. Intimal proliferation of the vessels and the occasional perivascular eosinophile also serve to differentiate solar dermatitis from chronic discoid lupus erythematosus. Collagen degeneration of the upper cutis as demonstrated on elastic stain is seen in chronic discoid lupus erythematosus. Similar changes may be seen in solar dermatitis. In lichen planus there is no tendency of the collagen to assume an elastic stain, but there is a complete loss of elastic within the cellular infiltrated zone.

In the rare controversial case it is necessary to rely on the clinical appearance of the lesions as well as the clinical course of the condition to arrive at a correct diagnosis.

DR. FRED D. WEIDMAN, Philadelphia: I would like to discuss first one of the larger aspects of the histological processes of lupus erythematosus, namely, whether the type of reaction is inflammatory or leucotic. Particularly in the chronic discoid form, the cellular infiltration lies in the correct position for a reticuloendothelial reaction at least, namely, in the lymphatic spaces around the blood vessels and the appendages, and I must confess that when I came fresh from general pathology to dermatology my first impression was that lupus erythematosus was of leucotic nature. However, I changed my mind promptly when I realized that proliferative reticuloendothelial tissue can be of inflammatory causation as well as leucotic, as in blastomycosis and in the chronic lesions of syphilis, for example. But it is the edema and the changes in the epidermis, I think, which contraindicate a leucotic factor; leucotic disease does not induce this type of change. That, of course, is cogent in connection with Dr. Harold Johnson's paper, read this morning, in which the possibility of a generalized reticuloendothelial disease featuring the spleen was implied. The reticuloendothelial hyperplasia does not of itself indicate a leucosis; it can still be inflammatory.

A further circumstance in point is the fact that not uncommonly, in both the chronic discoid and acute forms, there develops along the basement membrane a delicate line or zone of fibrinoid degeneration. I believe that it has not been recorded in print. It can be detected in hematoxylin and eosin preparations but is brought out spectacularly by the Hotchkiss-McManus stain. Fibrinoid degeneration of course is a function rather of inflammatory disease than of leucotic disease. I think this phenomenon should be pursued further in the analysis of the fundamental changes in lupus erythematosus. Perhaps it is comparable to the wire-loop changes which are seen in the kidney.

To turn next to certain details which are of importance in histologic diagnosis, may I discuss first the matter of "plugging." Simple dilatation, alone, of the hair follicle orifices is commonplace and does not constitute plugging. The plug must contain a relatively dense kind of keratinous matter, and the latter should preferably extend deeper down into the follicle. All of us know that the "large pores" of many persons are sufficiently large to result in very large and spectacular follicular orifices in sections.

Second, increasing numbers of cases of lymphocytoma cutis are coming to the laboratory with the question clinically of lupus erythematosus. This dermatosis has been advertised adequately lately, and is one of the foremost problems in the differential diagnosis of lupus erythematosus. Third, solar dermatitis is a large order and the whole story is not yet told. Not to belabor the matter, it is my main stumbling block in the laboratory. Finally, Dr. Ellis discussed the discrepancies between clinical and histologic diagnosis in his studies. I am sure that the true discrepancies are much smaller than he indicated and that if an adequate biopsy specimen had been supplied, his figures would shrink. If large, comprehensive, and appropriately selected biopsy specimens had been available on which to base his conclusions, the figures for discrepancies would have been lower. This is not a criticism of Dr. Ellis' work, but a commentary on the handicap which all pathologists suffer on account of inadequate biopsy materials.

DR. FRANCIS A. ELLIS, Baltimore: I wish to thank the discussers, and I would like to correct Dr. Beerman's quotation. He had an early copy of the paper. Instead of using the word, "will," I used the word "may," the "recurrent summer plaque-like 'may' show the same histologic picture as chronic discoid lupus erythematosus."

One of the interesting features in this study has been that we have been able to follow some cases that were considered from a clinical point of view by good dermatologists as lupus erythematosus and treated for several years as such, but in which the histology did not fit that picture. Eventually another diagnosis was made. I did not want to leave the impression that most of our biopsy specimens were only 2 mm. in diameter. They were not. We do have a few clinicians who take extremely small specimens, and really sections that small on an inflammatory disease are certainly a waste of time.

Dr. Weidman's speculation as to whether this is a leucocytic reaction or an inflammatory one is quite interesting. It is true that in some of the chronic discoids you have so much infiltrate and it is so uniform that it certainly suggests a lymphocytoma cutis, but ordinarily the epithelial changes help a great deal in the differential.

I think the fact that there is 60% agreement as to type of disease certainly would not make you say that the histopathology is diagnostic as to the type of disease, but 80 to 90% agreement as to the disease will suggest that the histology is certainly a valuable aid in diagnosis of this disease. I suggest that the pathologist take a little extra mental exercise by suggesting the type.

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ERYTHROMYCIN IN TREATMENT OF DERMATOSES

Report on 1,695 Patients

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THE INTRODUCTION of each new antibiotic offers a challenge to the clinical investigator to determine its value in the treatment of disease. To effect an impartial evaluation of the antibiotics in the treatment of dermatoses, a team of experienced dermatologists was formed in the Dermatology department at the University of Maryland. Diagnoses were confirmed in most cases by consultation with at least two other members of the team and, where indicated, by laboratory studies. Post-treatment observations were also confirmed by two or more of us. This same procedure had been applied to previously published reports on chlortetracycline (Aureomycin),[1] oxytetracycline (Terramycin),[2] and chloramphenicol (Chloromycetin).[3] In our initial studies, we found erythromycin to be of value in the treatment of granuloma inguinale,[4] and by local application, in the management of the pyodermas.[5]

Erythromycin is an antibiotic substance produced by an actinomycete which has been identified as a strain of Streptomyces erythreus on the basis of cultural characteristics, physiology, and microscopic morphology.

PATIENTS STUDIED

This report includes our observations on 1,695 patients with various dermatoses treated with erythromycin. Of these, 681 received the drug by mouth and 1,014 by local application of 1% ointment. The clinical material was obtained from the dermatology clinic of the University Hospital and our private practices. Since the results of the statistical evaluation were the same, no attempt is made to separate these individuals into age, sex, or racial groups.

From the Department of Dermatology of the University of Maryland School of Medicine.

This study was supported by grants-in-aid from The Upjohn Company, of Kalamazoo, Mich., and the Abbott Laboratories of North Chicago, Ill. Erythromycin used in this work was supplied by Dr. George Berryman of Abbott Laboratories and Dr. Harold Reames of The Upjohn Company.

PREPARATIONS USED

In our initial studies we found that erythromycin in plain gelatin capsules was ineffective, and this form of medication was discontinued in favor of special enteric-coated tablets, supplied in 100 mg. and 200 mg. tablets.

For local use an ointment was prepared using this formula.

Erythromycin	1.0
Heavy Mineral Oil	5.0
Petrolatum	94.0

PLAN OF TREATMENT

The general plan for both oral administration and local application was to treat each patient for a minimum of three weeks unless involution of lesions occurred or an adverse reaction developed. Placebos were used as controls in some chronic disorders or self-limited diseases.

TABLE 1.—*Oral Administration of Erythromycin: Dermatoses Definitely Benefited*

Disease	Total No. Cases	Good Results	No Improvement	No Follow-Up	Smallest Total Dose, Gm.	Largest Total Dose, Gm.
Abscess, superficial pyogenic	11	11	..	..	8	11.2
Cellulitis	48	45	..	3	8	16.8
Erysipelas	3	3	..	..	5.6	11.2
Erythema multiforme	31	21	5	5	11.2	17.6
Erythema multiforme bullosum	13	12	..	1	11.2	19.2
Furunculosis	23	21	..	2	11.2	22.4
Granuloma inguinale	14	13	..	1	8	22.4
Hydradenitis suppurativa	21	17	2	2	12.8	22.4
Lymphangitis	27	25	..	2	5.6	11.2
Pyoderma	21	20	..	1	5.6	11.2

ORAL ADMINISTRATION

All adults of average size were given 800 mg. of erythromycin daily, in enteric-coated tablets, divided into four equal doses. If no improvement was noted after three weeks, the drug was discontinued. In some dermatoses where improvement was noted, such as in acne vulgaris and acne conglobata, it was possible to reduce the dose to 100 mg. four times daily and still retain a satisfactory result. Children under 10 years of age were given a standard dose of 35 mg. per kilogram of body weight divided into four equal doses in a 24-hour period.

Results of Oral Treatment with Erythromycin.—The results of oral treatment may be divided into the three following categories: (1) conditions definitely benefited (Table 1); (2) conditions occasionally, partially, or temporarily improved (Table 2), and (3) conditions not benefited (Table 3). The drug proved to be of definite value (Table 1) in the treatment of those conditions in which there was involvement by pyogenic organisms, such as abscesses, cellulitis, erysipelas, furunculosis, kerion, hydradenitis suppurativa, lymphangitis, and pyoderma. An excellent result was obtained in 33 of 44 cases of erythema multiforme and erythema multiforme bullosum, and no recurrences have been reported after 3 to 6 months of follow-up. Rapid healing of all lesions of granuloma inguinale [4] was noted in 13 of the 14 cases treated, the remaining case being lost from observation. Administration

of the drug was continued for one week after all lesions healed. No relapses have been noted in this group of patients, although the shortest post-treatment period has been eight months.

One hundred ten patients (Table 2) with acne vulgaris, acne conglobata, and folliculitis were treated with erythromycin, and the large majority of these individuals improved while under treatment but relapsed when the medication was dis-

TABLE 2.—*Oral Administration of Erythromycin: Dermatoses Occasionally, Partially, or Temporarily Improved*

Disease	Total Cases	Partial Improvement	Temporary Improvement	Good Results	No Improvement	No Follow-Up	Smallest Total Dose, Gm.	Largest Total Dose, Gm.
Acne vulgaris	38	3	26	4	4	1	48.8	96
Acne rosacea	11	..	7	..	3	1	25.6	48
Acne conglobata	41	7	22	5	6	1	24	124
Dermatitis herpetiformis	2	..	2	..	..	..	24	48
Eczema, infected	35	23	6	..	2	4	5.6	11.2
Epidermophytosis, infected	19	17	..	..	1	1	5.6	16.8
Folliculitis	31	4	19	4	2	2	11.2	24
Infectious eczematoid dermatitis	28	..	17	2	5	4	11.2	24
Sycosis vulgaris	15	4	4	4	3	..	11.2	16.8
Tinea capitis, infected (kerion)	17	11	..	5	1	..	5.6	16.8

TABLE 3.—*Oral Administration: Conditions not Benefited*

Disease	Total Cases	Disease	Total Cases
Acne keloid	2	Lupus erythematosus, chronic discoid	8
Alopecia areata	6	Miliaria rubra	6
Aphthous stomatitis	10	Molluscum contagiosum	6
Atopic dermatitis	15	Otitis externa	5
Condylomata acuminata	4	Paronychia	8
Dermatitis venenata	8	Pityriasis rosea	12
Neurodermatitis	10	Psoriasis	12
Eczema, nummular type	15	Rosacea	4
Epidermophytosis	15	Sarcoid	2
Epithelioma	2	Scleroderma	1
Erythema nodosum	6	Seborrheic dermatitis	6
Folliculitis decalvans	2	Tinea capitis	6
Granuloma annulare	4	Tinea versicolor	4
Herpes simplex	12	Trichophytosis corporis	4
Herpes zoster	12	Verruca vulgaris	6
Keratosis follicularis	1	Verruca plantaris	6
Lichen planus	6	Verruca plana juvenilis	4
Lichen sclerosis et atrophicus	2		

continued. When treatment was reinstituted, these patients again showed improvement, and it was possible in many to maintain a satisfactory result by administration of a maintenance dose of 100 mg. three times a day. Similar results were noted in two cases of dermatitis herpetiformis. The antibiotic proved to be of definite value in controlling secondary pyogenic infection in cases of eczema, seborrheic dermatitis, epidermophytosis, and infected tinea capitis, but emphasis must be placed on the fact that while the secondary pyogenic infection was rapidly eradicated, there was no beneficial effect on the primary dermatosis. As noted in Table 3, many dermatoses failed to show a satisfactory response to the administration of the drug. In

self-limited conditions such as herpes zoster or pityriasis rosea, it is impossible to evaluate critically the effect of any drug unless dramatic improvement invariably follows the initiation of treatment.

Adverse Reactions to Oral Administration of Erythromycin.—In this series of 681 patients treated with erythromycin no adverse effect was noted on the blood picture. Seven patients complained of nausea; 3 had nausea and vomiting; 23 had diarrhea, and 1 had vague abdominal discomfort. It was necessary to discontinue the administration of the drug in 10 patients because of gastrointestinal symptoms.

TABLE 4.—*Local Application of Erythromycin: Dermatoses Definitely Benefited*

Disease	Total Cases	Good Results	Poor Results	No Follow-Up	Time Required for Good Results (Days)	Adverse Reactions
Abscess, draining	9	9	..	..	7 to 14	..
Dermatitis repens	18	16	..	2	7 to 21	..
Ecthyma	97	83	..	14	10 to 21	1
Impetigo contagiosa	221	193	..	28	3 to 14	..
Pyoderma	54	41	4	9	7 to 21	..
Purulent paronychia	2	1	..	1	14	..
Otitis externa	14	9	2	2	6 to 14	1
Sycosis vulgaris	19	16	2	1	7 to 21	..

TABLE 5.—*Local Application of Erythromycin: Dermatoses Occasionally, Partially, or Temporarily Improved*

Disease	Total Cases	Partial Improvement	Temporary Improvement	Good Result	No Improvement	No Follow-Up	Adverse Reaction
Acne vulgaris	15	..	6	..	9	..	..
Atopic dermatitis, infected	39	5	27	..	..	6	1
Contact dermatitis, infected	136	95	9	15	4	11	2
Eczema, stasis, infected	3	1	1	..	..	0	1
Epidermophytosis, infected	32	21	3	5	1	1	1
Folliculitis	11	3	3	3	1	1	..
Infant eczema, infected	24	15	4	..	2	2	1
Infected wounds and desiccation	11	8	..	3	..	..	..
Infectious eczematoid dermatitis	40	8	15	12	1	3	1
Insect bites, infected	11	1	5	1	..	1	..
Perlèche	2	1	..	1	..	..	..
Seborrheic dermatitis, infected	29	21	2	2	..	2	2
Stasis ulcer, infected	4	3	1	..	..	..	..
Tinea kerion	19	12	..	5	..	2	..

LOCAL APPLICATION

Early in this study a small number of patients with one of the pyodermas was treated with 0.5% erythromycin ointment but the results were not encouraging. Satisfactory results were noted when the strength of the ointment was increased to 1%. This preparation was used in the treatment of 1,014 patients with various dermatoses.

Results of Local Treatment with Erythromycin.—The results of the local treatment of dermatoses with erythromycin ointment may be divided into three categories: (1) conditions definitely benefited (Table 4); (2) conditions occasionally, partially, or temporarily improved (Table 5), and (3) conditions not benefited (Table 6).

Erythromycin ointment was of definite value in the treatment of the pyodermas (Table 4). Patients with impetigo contagiosa and ecthyma improved rapidly with complete involution of lesions in 3 to 14 days, depending on the severity of the condition. In all other conditions caused by pyogenic organisms similar results were obtained.

In many conditions such as eczema, epidermophytosis, atopic dermatitis, contact dermatitis, wounds, seborrheic dermatitis, and insect bites, where the primary dermatosis was complicated by secondary pyogenic infection, erythromycin ointment had no effect on the primary condition but caused rapid eradication of the secondary infection (Table 5).

As noted in Table 6, there were many dermatoses which did not respond to the local application of erythromycin.

Adverse Reactions to Local Application of Erythromycin.—No adverse reactions were encountered which could be attributed to the local use of erythromycin. Eleven

TABLE 6.—*Local Application: Conditions Not Benefited*

Disease	Total Cases	Disease	Total Cases
Atopic dermatitis	31	Papular urticaria	7
Alopecia areata	8	Pityriasis rosea	12
Dermatitis venenata	15	Psoriasis	12
Eczema, lichenoid (neurodermatitis)	11	Rosacea	4
Eczema, nummular	10	Scabies	2
Eczema, perianal	10	Seborrheic dermatitis	12
Epidermophytosis	14	Tinea capitis	8
Epithelioma	1	Tinea corporis	4
Folliculitis decalvans	2	Tinea cruris	4
Fox-Fordyce disease	2	Tinea versicolor	2
Granuloma annulare	4	Verruca acuminata	2
Herpes simplex	5	Verruca vulgaris	3
Herpes zoster	7	Verruca plana juvenilis	2
Lupus erythematosus, chronic discoid	4	Verruca plantaris	2
Molluscum contagiosum	4		

patients developed local irritative reactions to the ointment base but had negative patch tests to the antibiotic.

SUMMARY AND CONCLUSIONS

In this study, 1,695 patients were treated with erythromycin, administered orally to 681 patients and topically to 1,014.

Erythromycin in enteric-coated tablets proved to be of definite benefit in the treatment of all conditions in which pyogenic organisms were the primary cause of the disease.

Orally administered erythromycin was also of value in the eradication of secondary pyogenic infection from dermatoses such as atopic dermatitis, epidermophytosis, and seborrheic dermatitis, but had no beneficial effect on the primary disease.

Rapid involution of lesions of granuloma inguinale occurred following institution of erythromycin therapy. This drug also proved to be of value in the treatment of erythema multiforme.

Erythromycin may be considered as an adjunct to the therapy of acne vulgaris, but it does not replace any of the standard methods of treatment in use at this time.

No blood dyscrasias were noted in this series of patients treated with erythromycin orally.

Erythromycin ointment caused rapid healing of pyogenic infections such as impetigo contagiosa and ecthyma. It was also of value in the treatment of many dermatoses complicated by secondary pyogenic infection but had no effect on the primary dermatosis.

No adverse reactions were encountered which could be attributed to erythromycin on local application.

This drug is a valuable addition to the antibiotics already in use in the treatment of dermatoses, but, as with all antibiotic drugs, it should be used only where there is a specific indication.

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HERPES GESTATIONIS (DERMATITIS HERPETIFORMIS)

Report of a Case

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HERPES gestationis is a comparatively rare dermatosis occurring during pregnancy or the puerperium. The disease was described by Bunel in 1811, and the term herpes gestationis was suggested by Milton in 1872. Duhring believed that the disease belonged to the syndrome he had described under the name of dermatitis herpetiformis. The generally accepted opinion of most writers is that herpes gestationis is a variant of, or identical with, dermatitis herpetiformis. The relation to pregnancy is a characteristic of the disease not observed in dermatitis herpetiformis. This may indicate an endocrine relationship as suggested in the cases reported by Rostenberg,[1] Elliott,[2] Muller and Lapp.[3]

The infrequency of this disease is indicated by the reports of Perondi who found only 5 cases among 22,000 pregnant women, and Crawford,[4] 11 cases in 49,254 deliveries. Muller and Lapp,[3] in their review of the American literature for a 10-year period from 1934 to 1944, collected 15 cases and found mention of 18 others. They reported 2 additional cases, for a total of 35. In recent years, there has been only an occasional single case report.

The onset of the disease is often preceded by pruritus without cutaneous lesions. The dermatitis usually appears in a single or a few areas over the abdomen, about the umbilicus, the arms, or legs. Erythematous areas develop papules or urticarial lesions, single or grouped vesicles, or bullae occur in crops to produce the characteristic polymorphic appearance. The erythematous and vesicular areas increase, producing annular and gyrate lesions with scaling and pigmentation. The pruritus is persistent and at times extremely severe. There are periods of improvement, with recurring crops of vesicles, bullae, and large denuded surfaces.

The sulfonamides,[5] progesterone,[6] and adrenocorticotrophic hormone,[7] or cortisone [8] have been reported as useful therapeutic measures.

REPORT OF A CASE

B. W., a white woman, aged 33, in the eighth month of her third pregnancy. Her past and family history were irrelevant. Previous pregnancies were without abnormal incidents. Three weeks before term, an erythematous area developed about the umbilicus. There were a few papules and small vesicles over the abdomen. There was delivery, at term, of a normal viable male child by low forceps on Sept. 5, 1951. Mother and child were Rh-positive.[9]

The patient was first seen 24 hours after delivery. There had been rapid development of papules and vesicles over the abdomen, arms, and legs. There were extensive lesions over the

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Read before the Seventy-Fourth Annual Meeting of the American Dermatological Association, Inc., White Sulphur Springs, W. Va., April 16, 1954.

hands and feet; many were infiltrated and urticarial; some were annular and of iris type. Bullae were present over the palms and soles; itching was intense and especially severe over the hands and feet. During the next few days, there were many large bullae extending from the hands and feet to the legs, arms, body, and face. New papules and erythematous annular areas occurred which developed vesicles in the borders. There was considerable edema of the feet and legs. During the next three weeks, successive crops of papules, annular lesions, vesicles and bullae occurred with drying and healing, but followed by new lesions. The itching and discomfort were severe. Diphenhydramine (Benadryl), oxytetracycline (Terramycin), and sulfapyridine were of little benefit.

On Sept. 30, 1951, cortisone was administered orally, 200 mg. the first day, and 100 mg. daily for four days. Rapid improvement occurred, and only a few new bullae developed and the older lesions began to heal. Cortisone was gradually reduced to 50 mg. daily and then discontinued. There was a rapid recurrence of vesicles and large bullae, with intense itching. Cortisone, 150 mg. given daily for three days, again produced rapid improvement.

During the next four months, the dermatitis could be controlled by adequate dosage of cortisone, and usually 50 mg. daily would maintain a remission. There was recurrence of the lesions when the drug was discontinued.

Laboratory Report.—Blood Type: A, Rh-positive; Genotype, CDe/cDE. Infant: Blood Type, O, Rh-positive; Genotype, CDe/cDE. X-L Frog Pregnancy Test: negative after 24 hours.

Sulfapyridine failed to give improvement on several occasions. Progesterone, 100 mg. daily by intramuscular injections, was not beneficial and was discontinued because of painful nodules. Lingual progesterone was not helpful.

On Feb. 12, 1952, solution of potassium arsenite was started, 3 minims (0.185 cc.) daily with 1 minim (0.062 cc.) daily increase to 8 minims (0.493 cc.). Lesions healed and remained clear much of the time, but occasional crops of small vesicles occurred. A few lesions of the buccal mucosa developed during the next four months. There was pigmentation of the healed lesions.

May 8, 1952, β-pyridil carbinol tartrate (Roniacol Tartrate), an ethylated derivative of nicotinic acid, 100 mg. given four times daily, was beneficial in the control of the dermatitis. Only a few vesicles were present at the end of a week, and itching was relieved. There was flushing and burning of the face and arms for a few minutes after the medication. This preparation was continued in varying dosage until July, when 100 mg. given daily maintained almost complete remissions. The drug was discontinued in October, when the patient was free of itching, with only a few papules and occasional vesicles.

During the next six months, without medication, there were occasional groups of small vesicles usually at the time of menses. These mild recurrences were relieved in a few days on return to β-pyridil carbinol tartrate, 50 mg. taken two or three times daily. In April, 1953, she was free of lesions except during the menstrual periods. In February, 1954, she reported that she continued to have a few vesicles on occasions associated with the menses. She was free of vesicles during the entire month of February for the first full month in two years.

COMMENT

A patient with herpes gestationis developed a generalized vesicular and bullous dermatitis rapidly after delivery. The dermatitis was difficult to control. Sulfapyradine and progesterone did not produce benefit. Cortisone gave rapid relief with prevention of new lesions. There was rapid recurrence when the drug was discontinued. Cortisone was continued for four months, and no untoward metabolic or endocrine disturbances were observed. Fowler's solution was beneficial in reducing the activity of the disease during the next three months. β-pyridil carbinol tartrate [10] maintained remissions most of the time over a period of six months; the dosage was reduced from 400 mg. daily to 100 mg. as the process became less active and then the preparation was used only on occasions of new lesions.

SUMMARY

A patient with herpes gestationis which became generalized during the puerperium and persisted for more than two years is reported. There is considerable evidence that herpes gestationis is a variant of dermatitis herpetiformis.

Medical Arts Building.

ABSTRACT OF DISCUSSION

DR. LESLIE M. SMITH, El Paso, Texas: I believe that most dermatologists regard herpes gestationis as dermatitis herpetiformis occurring during pregnancy and the puerperium, that is, precipitated by the pregnant state. In this category should be included only those cases having the characteristics of dermatitis herpetiformis, such as the case reported by Dr. Fox. These cases, in my experience, are extremely rare.

More common among the dermatoses of pregnancy are the cases of papular urticaria, presenting an occasional vesicle, occurring usually during the latter part of pregnancy and clearing up soon after delivery. They may or may not recur during successive pregnancies, and not between them. Some consider this type of eruption a variant of dermatitis herpetiformis, but that is open to question. Personally, I believe that the two eruptions are unrelated, except in so far as they are both precipitated by pregnancy. True dermatitis herpetiformis of pregnancy may recur after the termination of pregnancy, especially at the menstrual periods, but it most often remains dormant until a subsequent pregnancy.

A discussion of herpes gestationis, in the present state of our knowledge, must be a discussion of dermatitis herpetiformis. It seems most likely that this disease is a virus infection which affects some persons with clinical signs and symptoms a large part of the time unless controlled with drugs, but which in others becomes active only when other disorders are present to lower the resistance or in some other way to make the system more susceptible to the virus infection, and which is capable of long remissions in the absence of these factors. While this is admittedly theorizing, this hypothesis seems plausible in view of the habit of repeated recurrences of herpes simplex, an accepted virus disease, during digestive disorders, febrile diseases, excessive exposure to sunshine, and a variety of other factors. Similarly, it may well be that dermatitis herpetiformis, or herpes gestationis, although probably of virus origin, becomes active when a factor is present which in some way lowers the resistance to a dormant virus infection. The importance of focal infection in this disease is well recognized, and the few cases I have seen permanently relieved have been those in which some focal infection was found and eliminated. Progesterone deficiency may be one of the factors predisposing to herpes gestationis, as suggested by the work of Keaty, Jones, and Lamb. Cawley and his co-workers have indicated the possibility of Rh-isosensitization in an Rh-negative mother being a factor in some cases. It appears reasonable that these and other factors might furnish the background upon which a subclinical virus infection becomes clinically evident, rather than that any of them is the real cause of the disease.

One might ask, if this is a virus infection, why it is so often controllable with sulfapyridine, which apparently has no effect upon other known virus infections. It has been questioned by Philpott and Woodburne, and others, whether the effect of sulfapyridine on dermatitis herpetiformis is a sulfonamide effect. Three of the drugs used more or less successfully in this disease, sulfapyridine, nicotinic acid, and β-pyridil carbinol tartrate, all contain the pyridine radical. Might it not be that the beneficial action of these drugs is due to their pyridine content, rather than to the sulfonamide?

One is jusified in concluding that the interesting case of herpes gestationis reported by Dr. Fox represents an example of true dermatitis herpetiformis, and one feels, more than ever, that the two conditions are the same.

DR. EDWARD P. CAWLEY, Charlottesville, Va.: Herpes gestationis is an intriguing disorder, as Dr. Fox has indicated. During the past three years, we have assembled some data which suggest that isosensitization by the Rh factor may be a causative agent in at least some cases of herpes gestationis. As you know, isosensitization by the Rh factor is the recognized etiologic agent in most cases of erythroblastosis fetalis and in some hemolytic transfusion reactions. The Rh factor acts as an antigen in those persons who become sensitized to it and they develop anti-Rh antibodies. The Rh-negative person may become sensitized in one of several ways; for example, an Rh-negative mother bearing an Rh-positive fetus, or an Rh-negative person given

a transfusion or intramuscular injection of the Rh-positive blood. The presence of anti-Rh antibodies and Rh-positive red cells in the same body gives rise to illness. The classic example of such a combination occurs when a sensitized Rh-negative person is given a transfusion of Rh-positive blood, resulting in a hemolytic transfusion reaction. Another example is that in which an Rh-positive fetus receives anti-Rh antibodies from the sensitized Rh-negative mother, resulting in erythroblastosis fetalis. An identical but less momentous combination, from the quantitative standpoint, may occur in the sensitized Rh-negative mother bearing an Rh-positive fetus during the latter half of pregnancy, when minute quantities of fetal blood presumably pass the placental barrier and enter the maternal circulation, and it is this combination, we believe, which may account for some cases of herpes gestationis.

Dr. Nelson Paul Anderson, Los Angeles: About two and a half years ago, I had the privilege of seeing this patient in Dr. Fox's office. I think that his viewpoint that herpes gestationis is related to dermatitis herpetiformis is the generally accepted one. The clinical features, the sequence of events, the response to therapy, all would seem to indicate that this is so, at least in this case. However, I should like to point out that there are those who believe that they are different disorders.

I should like to ask Dr. Fox if, in his search of the literature, he has found any instance in which a woman has suffered from typical dermatitis herpetiformis for years or for any length of time and then, for the first time, has become pregnant. If so, what happens to the eruption? I have never been able to find such a report, but surely such a sequence of events must have happened.

I also feel that in all cases in which there is any suggestion of anything less than the classic picture of dermatitis herpetiformis, a biopsy should be done. In the past year, I have seen one case in which the typical clinical features of dermatitis herpetiformis were present, and, on biopsy, the condition proved to be a benign familial pemphigus.

Finally, in those cases in which one is unable to use either sulfapyridine because of sensitization reactions or the corticosteroids because of contraindications, such as diabetes or high blood pressure, I would like to suggest the use of nicotinic acid in quite large doses. This medication will not necessarily cure the condition but will often at least ameliorate it to make it bearable. By very large doses, I mean doses of 300 to 400 mg., three or four times a day. If this is taken after meals, there is little, if any, of the unpleasant vasomotor reaction.

Dr. John G. Downing, Boston: In 1949, Dr. Jillson and I reported a case of herpes gestationis, and presented a statistical review of 20 cases appearing in 13 women. (Downing, John G., and Jillson, O. F.: Herpes Gestationis: Fetal-Anomaly Syndrome Treated Successfully with Sulfapyridine, *New England J. Med.* **241**:906 [Dec. 8] 1949). The average time of onset was five and three-tenths months of pregnancy. Eight of these women had histories of fetal anomalies. It was observed that if the fetal anomaly was a spontaneous abortion there was no associated herpes gestationis, because the uterus was emptied before the stage of pregnancy in which this disease had its onset. It might be postulated that some cases of spontaneous abortion of unknown etiology are due to this syndrome of fetal anomalies and herpes gestationis. Only if these patients had future pregnancies extending beyond the period of gestation in which herpes gestationis has its onset could the diagnosis of the disease be made.

One of my patients had three attacks, each almost simulating a typical pemphigus. She became pregnant for the fourth time and had no eruption, but delivered a child with congenital heart disease.

In all the cases I have seen, the eruption has cleared within a few weeks or months after delivery.

Dr. John H. Lamb, Oklahoma City: We had one case of herpes gestationis which was post partum out of our series. The patient had had a previous pregnancy and in this pregnancy had suffered with the disease rather severely for four months post partum. With her second pregnancy, we used 50 to 100 mg. of progesterone parenterally daily for six weeks and the symptoms were completely controlled.

These postpartum cases are difficult to explain. Some are thought to be retained placenta or derived from chorionic growths. Our cases during pregnancy showed an unusually high level of chorionic gonadotropins and the skin manifestations were controlled by progesterone. However, I think that Dr. Fox's patient had a negative reaction for gonadotropins (frog test).

I should like to recommend anhydrohydroxyprogesterone (Pranone), an oral progesterone, 25 mg. a day, beginning 10 days before each period, to relieve the recurrent herpetic menstrual flare in Dr. Fox's interesting case.

DR. BEATRICE M. KESTEN, New York: In support of Dr. Cawley's theory of autosensitization, may I tell you the history of a mother with a similar eruption?

During her first pregnancy, a transfusion was required. In the fifth month of her second pregnancy she first developed an eruption similar to that just described by Dr. Fox. At this time she was found to be Rh-negative and her husband Rh-positive. The eruption cleared promptly after delivery of a normal child. During the fourth month of her third pregnancy, the eruption reappeared and worsened as her pregnancy progressed. There was no improvement with oral sulfapyridine and a patch test with 50% potassium iodide was negative. Histologic examination of one of the vesicles showed only a nonspecific dermatitis. Three weeks before term, her blocking antibodies had reached 1:64 and she was delivered of a normal baby. Within a few days the eruption subsided. During the last five years she has had no pregnancies and no eruptions.

DR. EVERETT C. FOX, Dallas, Texas: In looking over the literature, I would assume there are at least 100 cases readily available for reference at the present time, and I know there must be many more that are unreported. This condition represents a stress of pregnancy, a toxemia, or an endocrine dysfunction as the mechanism that sets off a dermatitis herpetiformis of these particular characteristics during pregnancy. There do seem to be two distinct groups. There are those that occur during the early periods of pregnancy or in the last trimester and that promptly improve with delivery; these apparently are never as severe. The more severe ones come on insidiously and in the last month or two of pregnancy. They flare up explosively at the time of delivery. This type has a tendency to persist for prolonged periods—6, 9, or 12 months. There was one case of 12 months and one of 9 that I was able to find reported. The cases that occur at delivery are more prolonged and are frequently more severe.

I have been unable to find a case, Dr. Anderson, of a patient having dermatitis herpetiformis who was treated prior to pregnancy and then observed during pregnancy.

It is interesting, in looking over the literature, to see that the group in Boston reported 25 cases in 50,000 deliveries, but almost within the same month, one of the men in the department of obstetrics reported that no case had occurred in their institution in the same period of years.

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SOME HISTOLOGIC ASPECTS OF CERTAIN BULLOUS DISEASES

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THE HISTORIC aspects of the histology of the bullous diseases and the accompanying casuistics have been thoroughly reviewed by Civatte, Lever,[1] Director, and others.* It still is a puzzle to me as to why the microscopic picture and pathologic morphology of these conditions, which so many observers today regard as diagnostic, were not appreciated by earlier masters, who looked for the very features to which so much positivity is nowadays attached, and who looked for them in relation to the clinical pictures.

Now, recognizable clinical entities exist only if recognizable patterns recur with a measure of regularity; otherwise we have nothing but hopeless chaos. If there is in addition a measure of regularity and parallelism between the clinical patterns and the histologic findings, then, and then only do the microscopic features of accepted "clinical entities" have meaning for us. I, therefore, take for granted the recognition of the existence, as distinct entities, of the following complexes, which I shall discuss: pemphigus vulgaris, Duhring's disease (its bullous form), erythema exudativum multiforme, and a more heterogeneous group, which includes pemphigus-like, dermatitis-herpetiformis-like, and erythema-multiforme-like bullous conditions, which are, nevertheless, none of these three diseases, and are probably in many cases drug eruptions. To these must, for special reasons, be added Hailey-Hailey's disease (which in my opinion is not a bullous form of Darier's disease). For the sake of brevity, I must exclude acute, so-called butcher's pemphigus, epidermolysis bullosa, and the many other bullous dermatoses from this discussion.

The three microscopic methods which have, in recent years, been utilized for the study of the bullous diseases are (1) standard fixation and staining, by Civatte and others; (2) cytologic examination, with quick fixation and staining of scrapings, smears, and bulla contents, by Tzanck and others, and (3) polarization microscopy, by Nieuwmeijer.

STANDARD FIXATION AND STAINING

Without entering into an analysis of the older literature and the pendulum of opinion as to the feasibility of the histologic differential diagnosis of the bullous conditions, I would point out that Auspitz, as early as the 1880's, coined and

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* In view of the comprehensive bibliography published in Lever's article, I am excluding bibliographic notes almost completely.

used the terms acantholysis and acantholytic bulla and referred to the cachectic (now called degenerated) nature of the affected cells in pemphigus, in contrast to findings in the other bullous diseases.

The majority of modern dermatopathologists have closely followed Civatte, since his article, published in 1943, and opinion has been crystallized with minor variations.

Accordingly, in pemphigus vulgaris there is always intraepidermal, usually suprabasal, acantholysis and bulla formation, often irregularly shaped, never primarily subcorneal or subepidermal, though the bulla may become so, partly or secondarily, with age or by diverticulation. Detachment of isolated or grouped epithelial cells takes place. These are degenerated and have lost their prickles. They may resemble balloon cells or take on other forms, which have been variously described by different authors, indicating that these detached cells are by no means of uniform type. Intraepidermal acantholysis of the follicular walls, seen in sections of the follicles deep in the cutis, is, when found, perhaps the single most reliable diagnostic feature of pemphigus. Acanthosis and papillomatosis, sometimes seen early in pemphigus vulgaris in its transition to the vegetans form, may occur in Hailey-Hailey's disease. They are only rarely found in Duhring's disease, but not in erythema multiforme or the pemphigus-like eruptions. However, further discussion of pemphigus vegetans and foliaceus, interesting though they may be, is not pertinent here, because they do not present problems of differential diagnosis from the other bullous diseases. However, I must emphasize that I agree with the concept of the essential unity of pemphigus vulgaris, vegetans and foliaceus.

According to Civatte and his followers, in Duhring's disease the bulla is always subepidermal, usually regular in shape, formed by sudden uplifting of the epidermis from the cutis, with stretched, not acantholytic cells at the periphery of the bulla. Detached epidermal cells are not found or are only sparsely found in the bulla, and such as are present are not degenerated. The bulla may become partly intraepidermal by diverticulation, or epidermal cells may be found on the sides of the floor of the bulla during stages of repair.

In erythema multiforme, Civatte described the abrupt tearing off of the epidermis from the cutis, so that an irregular bulla is formed, which is mainly subepidermal, though clumps of epidermal cells may still adhere to the papillae. The site of the bulla and the adjacent epidermis show intense necrosis of cells, and the bulla may contain vestiges of epidermal elements. Civatte considered the differences between Duhring's disease and erythema multiforme to be definitive; others are unable to find satisfying criteria with useful regularity.

Now a few words about the cutis and inflammatory features. In all three diseases there may occur such variety in quality and quantity of cellular infiltrate that this has little diagnostic value. In pemphigus, it may vary from minimal cellular reaction to heavy infiltrate of polymorphonuclear neutrophiles, eosinophiles, histiocytes, and small round cells in the upper cutis, as well as mixed with the detached epidermal cells in the bulla. Eosinophiles may predominate.

In Duhring's disease, the same variety may be found; though here eosinophiles in the cutis and bulla are more common and predominant.

In erythema multiforme, the cellular infiltrate may be slight to heavy; extravasated red blood cells may be found. Civatte saw no eosinophiles; others have found them in small numbers in the cutis and the bulla. I think that intense edema of the upper cutis is, when seen, more characteristic of erythema multiforme than of Duhring's disease or pemphigus.

Other conditions which, for one reason or another, cannot be placed with these three diseases and which are variously known as bullous pemphigoid (although the term pemphigoid should be reserved for the bullous staphylogenous impetigo), pemphigus vulgaris chronicus (a poor name), erythema bullosum, or toxic bullous eruption present more difficulty. Those who claim specificity for the histologic pictures of pemphigus, dermatitis herpetiformis, and bullous erythema multiforme agree that erythema bullosum can be clearly differentiated only from pemphigus, but not from Duhring's disease and erythema multiforme. On this account some authors regard erythema bullosum as a variety of one or other of these last two. Others are inclined to lump Duhring's disease and erythema multiforme together.

CYTOLOGIC DIAGNOSIS

The program of the establishment of the Inter-Society Cytology Council [2] reads: "The ideas of those who have concerned themselves with the development of this organization are based upon the following convictions . . . the cytologic diagnosis of cancer should not be accepted as conclusive. Biopsy still remains the method of final diagnosis." I would express a similar idea in a modified way, that cytologic examination, interesting though it be, should not replace biopsy examination, nor can it give the information that may be afforded by a biopsy examination. If a biopsy specimen with its architectural aggregate is not conclusive (and it is certainly not fool-proof) in many cases, then surely reliance should not be placed on cytologic and necessarily fragmentary examination. This holds true particularly in skin conditions, cancer as well as bullous diseases, for here we have a tissue that lends itself so easily to more adequate investigation.

Since Tzanck published his findings in examination of scrapings from the floor of the bulla in various conditions, there has been further considerable unanimity of opinion, some investigators using scrapings, other smears, and others bulla fluid. The main feature is that in pemphigus there are many isolated as well as clumped, acantholytic, degenerated epidermal cells. Most observers describe a large nucleus, others an amorphous pyknotic nucleus. Some see resemblance to balloon cells, others see distinct differences from them. At all events the cells are degenerated and do not show mitoses. The cytoplasm is a relatively narrow rim, with condensation of material at the periphery of the cell, and perinuclear diaphany may be seen. Similar but milder effects are seen in Hailey-Hailey's disease, but in no other bullous eruption. Most cytologic investigators agree that although the findings in pemphigus are differentially diagnostic from the other bullous diseases, the latter cannot be cytologically distinguished from each other. In dermatitis herpetiformis, detached, but otherwise normal, epidermal cells may be found, not uncommonly with many eosinophiles, and with varying numbers of histiocytes, blood cells, lymphocytes, and fibrin. In erythema multiforme, the material examined showed some neutrophiles and lymphocytes, with occasional eosinophiles. The inconstancies are too frequent to allow absolutism of interpretation.

POLARIZING MICROSCOPY

Nieuwmeijer[3] studied bullae with the polarizing microscope. His material, a total of 19 cases, was, in my opinion, not adequate for reliable conclusions. However, he found that the sub- or intraepidermal location of the bulla did not take strictly formalized lines of cleavage. Fatal pemphigus might show subepidermal bullae throughout the course of the disease, while Duhring's disease might show acantholysis.

Usually in pemphigus the bulla is irregular in outline, with no tension and no stretching of surrounding cells. There is intracellular edema of the affected cells, with shrunken nuclei (*grains cornés*) and acantholysis, though according to Nieuwmeijer this is not specific for pemphigus and may be found in cantharides blisters. The tonofibrils disappear or are diminished in and also around the bulla, and are not pushed aside and concentrated at the periphery of the bulla as they are in dermatitis herpetiformis. In contradistinction to spongiotic vesicles, the floating cells in pemphigus bullae show no double refraction around the nuclei, indicating that the tonofibrils within the affected cells are destroyed, as well as those of the prickles. Nieuwmeijer found the same results in the scrapings from pemphigus bullae.

In Duhring's disease, the bulla is regular in outline and is due to tension. It may be either sub- or intraepidermal. Around the bulla the cells are stretched but otherwise normal. With polarized light, the epidermal elements adjacent to the bulla show concentration of doubly refractile tonofibrils, arching over to the roof. However, he also had cases in which the histologic findings did not parallel the clinical ones, and tension bullae were found up to the fatal termination of clinical pemphigus.

ANALYSIS AND CRITIQUE

We thus have three histologic methods which help us in differential diagnosis of the bullous diseases. I say help advisedly, because, in spite of the weighty and authoritative opinions on the definitive quality of their value, I for one, (and there are others), am not convinced of the finality of diagnosis made by histologic examination. Thus, I have seen completely subepidermal bullae in fatal bullous diseases, which clinically were nothing but pemphigus and were not to be classed with the other bullous dermatoses in cachectic or aged patients. One can argue that the biopsy specimens were not well chosen or taken, that serial sections were not made, and that the lesions were old. But even when these contingencies are avoided, there still remain cases which cannot be pigeonholed histologically, any more than they can be clinically. I have seen intraepidermal or partly intraepidermal bullae in Duhring's disease and erythema multiforme. If it is argued that in such cases some of the bullae or parts of them might have been subepidermal and therefore primarily arose subepidermally, and that in cases of clinical pemphigus with subepidermal or partly subepidermal bullae some of the bullae or parts of them might have been intraepidermal, and therefore primarily arose intraepidermally, one is begging the question. Such arguments are obviously based on preconceptions of the inevitability of the primary subepidermal location of dermatitis herpetiformis and erythema multiforme bullosum and of the intraepidermal location of pemphigus. I agree that intraepidermal vesiculation with acantholysis is strong evidence in favor of pemphigus. But as

Caro [4] reminds us with sarcastic undertones: "The word acantholysis is already becoming the trigger word that at once points to the diagnosis of pemphigus." In doubtful cases of acantholysis (and there are many), and particularly those with partly subepidermal, partly intraepidermal vesiculation (and these are the ones which cause the headaches of clinical differential diagnosis), a corresponding group of histologic riddles is found. On the other hand, subepidermal vesiculation does not, in my opinion, rule out pemphigus.

Cytologic examination, as I have indicated, is at best only corroborative. The advantage of this method is that cellular structure is less distorted than by the ordinary methods of fixation and staining. Except for research purposes I can find little to recommend it. A biopsy specimen of a fresh bulla in toto usually gives much more valuable information.

Of the latest method, by polarizing microscopy, I have no personal experience. It may be another useful, but in all probability no more than useful, diagnostic aid. But I think it will help us understand the pathogenesis of the bullous diseases.

Our main stumbling block is that we have no absolute criteria wherewith to prove the correctness of the diagnosis of pemphigus, versus Duhring's disease, versus erythema multiforme bullosum, or versus the bullous diseases which simulate one or other of these diseases and which have been labelled by so many evasive terms. Now that death as a criterion for pemphigus is fortunately being removed in many cases, by the use of corticosteroids and corticotropin (ACTH), I feel that the final solution is likely to evade us, rather than be reached in time. Furthermore, a review of older literature is not helpful, because of this very lack of absolute criteria.

I would add a few words about Hailey-Hailey's disease versus pemphigus. Of course the clinical picture and course ordinarily distinguish them, so that the question is usually purely academic. In sections which I have examined I have found that intraepidermal acantholysis is an essential of Hailey-Hailey's disease. It is typically suprabasal. Moreover, in a given field one sees stratum over stratum of acantholysis, whereas in pemphigus there is in one high-power field usually only one layer of lacuna formation. Also, in Hailey-Hailey's disease, a whole high-power field of prickle cells may be affected, so that groups and isolated acantholytic cells may be seen, not only protruding into and floating in but also adjacent to the lacuna. These cells often have a glistening hyalinized appearance with hematoxylin and eosin stain. Nevertheless, such cells are apparently more viable than the separated cells of pemphigus, and mitoses are not uncommon in them. It is these cells that show the dyskeratotic forms or transitions to them. However, though the grain-link types are fairly common, and the *corps-rond* type may also be seen, neither of these two dyskeratotic cell varieties is a necessary feature of Hailey-Hailey's dermatosis.

It would seem to me that out of all the labyrinthine presentation we do get some basic facts. The epidermal cells in pemphigus are seriously affected. There is a dissolution of tonofibrils, which manifests itself within the cells as degenerative changes, seen in scrapings, smears, and bulla contents, and which is corroborated by the lack of double refraction around the nucleus on polarization. The tonofibrillar apparatus of the prickles is similarly affected; the cells therefore loosen individually or in clumps.

This offers an attractive explanation for the usually, but in my opinion not inevitably, intraepidermal, suprabasal location of the pemphigus bulla. With the dissolution of the tonofibrillar apparatus, the prickles of the Malpighian cells disappear on all sides, and the cells separate from their neighbors to form intraepidermal bullae. The cells of the basal layer, it is true, have projections, denticulated downward, that probably carry tonofibrillar elements, which contribute to, but do not totally account for, the adhesion of the epidermis to the cutis. Thus, although the cells of the basal layer are affected, and their prickles are involved, and the tonofibrillar elements of the underside undergo dissolution, the other adhesive factors are usually sufficient to hold them down. On the other hand, the tonofibrillar affection of the underside may be intense enough to lead to separation of the basal cells from the cutis, and thus form, primarily, a subepidermal bulla.

Further pursuit of the subject of the adhesion of the epidermis to the cutis, and its relation to the selective localization of bullae in other diseases, fascinating though it be, would lead far beyond space limits, and in any case is already involved in vast literature and wide investigation.

CONCLUSIONS

1. Completely intraepidermal, suprabasal, acantholytic, nontension bullae are, except for Hailey-Hailey's disease, practically diagnostic of pemphigus.

2. Subepidermal bullae do not exclude pemphigus.

3. Subepidermal tension bullae, with heavy eosinophilic infiltrate under and within them, are in favor of Duhring's disease.

4. Subepidermal bullae, which are associated with necrosis of the adjacent epidermal cells, especially if the upper cutis shows intense edema and extravasation of red cells, are in favor of erythema multiforme.

5. Bullae with signs suspicious of acantholysis, which are partly intraepidermal and partly subepidermal, or with heavy cellular infiltrates which confuse the detailed architecture, are not diagnostic, in spite of individual features, imagined or true.

6. No histologic picture should damn or label a patient without confirmation of clinical evaluation.

2 W. 87th St. (24).

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BONE LESIONS IN KAPOSI'S SARCOMA

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IN A RECENT report, Cajaffa [1] presented the case of a 29-year-old woman with cutaneous lesions of Kaposi's sarcoma, who, in addition, showed osteoatrophy of the bones of one foot. He then searched the literature on the subject and was able to find nothing except for the simple statement by Casuccio [2] that in hemorrhagic and vascular diseases, among them Kaposi's sarcoma, bony changes may be found. Cajaffa then looked for cases of Kaposi's sarcoma in the dermatology clinic of the University of Bari, Italy, and there found 16. Of these, only three were available for examination and all three demonstrated osteoporosis of the extremities on roentgenographic study. In commenting on these observations, he stated that the osteoporosis is localized either under the cutaneous lesions or at a point distal to them; that it is more marked the longer the duration and extent of the cutaneous lesions; and that, on the basis of studies on bone physiology by Leriche and Policard, the rarefaction was due to the increased circulation through the limb as a result of the cutaneous alterations.

Dorffel,[3] in 1932, reviewed the literature on Kaposi's sarcoma and, in contrast to Cajaffa, concluded that the skeletal system is frequently involved. Azulay [4] cited the reports of Schwimmer, Scholtz, Bernhardt, Feit, Halle, Mierzecki, Pick, Rash, and Zumbush, all of whom found bony alterations in patients with Kaposi's sarcoma. Grinspan [5] referred to Janselme and Huet, and Vigne and Fournier, who found bony decalcification in their patients. He stated that the characteristic x-ray picture is that of atrophy and decalcification.

Despite the numerous reports in the foreign literature, we have been able to find few cases of Kaposi's sarcoma with bone lesions described in the English literature. Kusnezow,[6] in 1933, reported on a 32-year-old man with Kaposi's sarcoma who complained of marked back pain and whose x-rays revealed definite atrophy of the bone substance within the third to fifth lumbar vertebrae. There were no cutaneous tumors on the back. At autopsy the lumbar vertebrae macroscopically showed softness and porousness and a grayish-red color of the marrow; microscopically, the marrow showed ordinary hemopoiesis and "unimportant lacunae formed at the expense of the long-oval cells of granulation type without any osteomyelitis accompanying this process of absorption." Aegerter and Peale,[7] in 1942, reported four cases of Kaposi's sarcoma, one of whom, a 63-year-old man, had nodules on the dorsum of the foot and toes; x-rays showed a soft tissue tumor

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invading the bones of the foot. In 1945, Nesbitt, Mark, and Zimmerman [8] reported a case of disseminated visceral lesions of Kaposi's sarcoma in the absence of cutaneous tumors. One of the findings at autopsy was tumor in the thoracic and lumbar vertebrae. The microscopic picture of the bone lesions was that of "a granulomatous hemorrhagic sarcoma with a pleomorphic spindle cell as the dominant structural unit." Collins and Fisher,[9] in 1950, presented the case of a 25-year-old man with Kaposi's sarcoma involving the vertebral and femur marrow in addition to other viscera and the scalp. In 1952, Sherwin and Gordimer [10] reported on a 61-year-old man with visceral and cutaneous lesions of Kaposi's sarcoma. Roentgenograms of the right foot and leg, which were sites of cutaneous tumors, showed considerable demineralization of the bones with what appeared to be a destructive process of the os calcis. The leg was amputated, and a longitudinal section disclosed a fungating growth extending from the skin through the muscles into the os calcis. Kaminer and Murray [11] found two cases of Kaposi's sarcoma with bone lesions in

Fig. 1.—Vascular lesions of Kaposi's sarcoma in a typical location, the foot. Unusual locations are the cutaneous-subcutaneous tumors of the thigh, groins, and abdomen.

the records of the South African Institute for Medical Research. The case reports were not complete, but in one it was mentioned that biopsy revealed Kaposi's sarcoma involving bone.

Although bone changes in Kaposi's sarcoma, judging from the foreign literature, are not rare, we are presenting a report of such a case to focus attention upon this phenomenon which, with the exception of the cases cited and simple mention of its occurrence in some reviews, has been largely ignored in the English literature. It is our hope that it will stimulate the roentgenographic study of patients with Kaposi's sarcoma.

REPORT OF CASE

J. P., a 33-year-old barber of Italian extraction, noted the appearance of a lesion of the right foot, in 1935, at the age of 15 years. This lesion was excised, but subsequently recurred in the site of excision and new nodules developed in the adjacent area. He was first seen by one of us (F. R.) in 1937, at which time several bluish nodules were present on the medial aspect of the right foot. A biopsy was reported as showing hemangioma.

Fig. 2.—Roentgenogram showing areas of rarefaction in the proximal phalanx of the left thumb and in the proximal phalanx of the left index finger.

Fig. 3.—Roentgenogram showing the area of rarefaction in the proximal phalanx of the right great toe.

Fig. 4.—Roentgenogram demonstrating phleboliths or calcium deposits within the blood vessels, a condition often seen in extensive hemangioma.

The diagnosis of Kaposi's sarcoma was made and treatment with radium given. The patient was not seen again until 1952, when he returned because of concern about a large lesion on the heel. Examination revealed a large, bluish, verrucous nodule on the medial aspect of the right heel, multiple bluish nodules over the right foot and ankle, and skin-colored nodules on the right thigh, abdomen, and scalp (Fig. 1). He was completely asymptomatic. Although a biopsy at this time was reported as showing fibroma, the diagnosis of Kaposi's sarcoma was incontestable.

In 1953 a complete skeletal x-ray series showed alteration of the bones of the left hand and right foot (Figs. 2 and 3). The x-rays of these parts were described as follows by Dr. Lawrence A. Martineau: "Examination of both hands shows no demonstrable soft tissue change. There is noted a cystic rarefaction involving the medulla of the shaft of the proximal phalanx of the left thumb. The trabeculae in this region show demineralization. The cortex is intact. There is noted a similar cystic area of bone atrophy and/or bone destruction involving the terminal end of this same phalanx. In addition, there is noted a very small cystic area, measuring no more than 2 or 3 mm. in diameter, involving the medial cortex of the proximal end of the proximal phalanx of the left index finger. The remaining bones of the hands show no definite abnormality. Examination of the feet shows numerous spotty calcific densities near the right talus and medial malleolus (Fig. 4). There are also a few of these calcific densities lying close to the proximal end of the first metatarsal and the proximal phalanx of the right great toe. These are thought to represent calcium within blood vessels in the soft tissues. There is noted one rarefied cystic area measuring about 0.5 cm. in diameter involving the proximal phalanx of the right great toe. The relation of these bony cystic areas to Kaposi's sarcoma is speculated."

Two other conditions which might produce bone changes resembling those observed in this case are gout and multiple myeloma. However, the patient had no signs or symptoms suggestive of either of these diseases, the blood uric acid was normal (3.0 mg. per 100 cc. of whole blood), and there was no evidence of Bence-Jones protein in the urine. The blood calcium and phosphorus per 100 cc. of serum were 5.6 mg. and 3.3 mg., respectively; acid phosphatase was 1.8 K. A. units and alkaline phosphatase was 4.4 Bodansky units.

In view of the patient's occupation as a barber, requiring the use of both hands and feet, a bone specimen was not obtained. However, in view of the absence of other likely causes and the presence of Kaposi's sarcoma, it was concluded that the osseous lesions were probably due to the latter disease.

COMMENT

Having accepted the fact that the bone changes were due to Kaposi's sarcoma, one may speculate as to the specific nature of these lesions.

An obvious possible cause of bone changes in patients with Kaposi's sarcoma is direct extension from soft tissue, as observed in the cases of Aegerter and Peale [7] and Sherwin and Gordimer.[10] This was not the pathogenesis in our case.

According to Cajaffa,[1] bone rarefaction results from increased blood flow through the part, in turn the result of the vascular cutaneous tumors. However, our patient showed involvement of the bones of the hand while lacking cutaneous lesions of the upper extremities. Similarly, the patients of Kusnezow,[6] Nesbitt and co-workers,[8] and Collins and Fisher [9] lacked cutaneous tumors in the region of the involved bones. Additional doubt may be cast upon Cajaffa's concept by the fact that of the 11 patients with Kaposi's sarcoma we have studied roentgenographically, only the one in the case reported had bone lesions, despite the fact that many of the others had cutaneous tumors which were much larger and more extensive. Furthermore, whereas blood flow through an extremity may be increased in the early stages of its involvement by Kaposi's sarcoma, it appears likely that in most cases as the disease progresses the circulation through the tumor-bearing area is decreased as a result of cellular infiltration and lymphatic obstruction.

As we have previously pointed out,[12] it is most probable that new lesions of Kaposi's sarcoma develop not as the result of metastasis, but rather through

autochthonous origin. A possible explanation for the bone lesions in patients with Kaposi's sarcoma is that they represent such new primary tumors. This pathogenesis would explain the osseous changes in the cases reported by Nesbitt and co-workers,[8] Kusnezow,[6] and Collins and Fisher.[9] Although in the absence of a confirmatory biopsy the statement cannot be made with finality, we do believe that the bone lesions in our case are probably also on such a basis.

SUMMARY

The literature concerning bone changes in patients with Kaposi's sarcoma is reviewed.

A case of Kaposi's sarcoma showing cystlike areas of rarefaction in the bones of the hand and foot is reported.

The pathogenesis of such osseous alterations is briefly discussed.

170 Waterman St. (6).

247 Waterman St. (6).

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NEGATIVE TEST FOR HEPARIN IN MAST CELLS OF URTICARIA PIGMENTOSA

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SINCE it became known that mast cells contain heparin or heparin-like material, speculation arose about the concentration of these potent enzymes in the skin of subjects with urticaria pigmentosa. It is said the same cells contain histamine, too, which would readily account for the ability of the skin to react by whealing on stroking or rubbing.

Recently investigators studied intensively the so-called "clearing factor" the body develops somewhere within itself when one injects heparin intravenously. This "clearing factor" removes the milky appearance of blood serum following a fat meal. However, the oldest and best-known property of heparin is its ability to interfere with coagulation of blood. Accordingly, a simple and direct test for the presence of heparin concentrates in the skin at the site of lesions of urticaria pigmentosa would be interference with the blood coagulation reaction by extracts of such skin. A positive test (interference) could be interpreted to mean that the tissue and presumably the mast cells in it contained heparin-like material.

An opportunity to put this to a test came when a white man, 42 years old, presented himself with an eruption of brownish macules, mostly on the trunk. The lesions urticated on rubbing. A diagnosis of the acquired form of urticaria pigmentosa was made. Histological examination corroborated the diagnosis. The sections contained a goodly number of mast cells.

METHOD

A piece of skin including a large lesion and part of another lesion was removed with scalpel. The specimen weighed 1.2 gm. It was minced into fine particles with a razor blade and ground up in a small quantity of fine-grained sand and mixed with 2 cc. of saline. This was centrifuged, and the supernatant liquid was added to blood for coagulation timing. Lee and White's method was used. One cubic centimeter of venous blood was mixed with 0.1 cc. of the supernatant liquid from the skin preparation and put into test tubes of 8 mm. diameter. Two tubes each were set up containing the patient's and my blood, and for each set the average time elapsing before one could invert the tubes without displacing the clot was recorded. Two weeks later, another piece of skin was removed from the patient's other side. It weighed 0.95 gm., and was treated the same way as the first.

Venous blood was drawn before and after rubbing large areas of the patient's skin, producing whealing. Clotting time calculated by Lee and White's method was determined for each of the two samples.

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RESULTS

Experimental error undoubtedly accounts for the variations in results, and thus the experiment did not demonstrate that the tissue extracts or blood after rubbing the skin contained any factor to delay blood coagulation.

COMMENT

These experiments do not disprove the presence of heparin or heparin-like materials within the mast cells of lesions of urticaria pigmentosa. Such substances could be there in an inactivated state, or another factor or set of factors necessary to activate the heparin may be missing. The other possibility, of course, is the

Coagulation Time of Blood in Patient with Urticaria Pigmentosa Compared with That in Normal Subject

	Coagulation Time, Minutes			
	Without Extract		With Extract	
Subject	1st Biopsy	2d Biopsy	1st Biopsy	2d Biopsy
Urticaria pigmentosa	6.5	5.0	7.0	6.0
T. C.	10.0	9.5	9.5	9.5

Coagulation Time, Minutes	
Before Rubbing Skin	After Rubbing Skin
6.5	6.0

presence of inactivators. It is assumed too, that the method employed was capable of extracting the postulated materials. It is evident heparin in the mast cells of urticaria pigmentosa in vivo does not exert its otherwise usual properties, else the patient's coagulation time would not be normal but prolonged.

SUMMARY

Two biopsy specimens, taken at different times from one patient with the acquired form of urticaria pigmentosa, yielded extracts incapable of prolonging the coagulation time of blood. The coagulation time of the patient's blood after rubbing a large area of his skin with the production of whealing was not longer than that of the sample drawn before rubbing. The conclusion seems warranted that heparin (or similar substances) in the mast cells of the lesions is in a form needing activation or that an inactivating substance interferes with its blood-anticoagulating action.

SEBACEOUS GLANDS IN THE TONGUE

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THE SEBACEOUS glands are prominent adnexal components of the skin, which are normally found either closely associated with hair follicles to form the pilosebaceous apparatuses, or are found independently, but nevertheless in areas of the skin where follicles are present in greater or smaller numbers. Their existence in such locations as the mucocutaneous areas and the buccal mucosa (Fordyce's condition) is well known, but their occasional presence has been recorded in many other ectopic sites. Ectopic sebaceous glands have been reported on the mucous membrane of the male genitalia,* on the mucous membrane of the female genitalia,† in the cervix uteri,‡ in the lacrimal caruncle,§ and in a polyp of the anterior commissure of the larynx.[18] Very rare cases of sebaceous cysts and sebaceous gland carcinoma, in such unusual sites as the palms and soles, are on record.|| Recently the presence of sebaceous glands apparently arising from the intercalated ducts of both normal and neoplastic parotid gland tissue, has been rather commonly observed by pathologists.¶ In an extensive review of the literature, we were unable to find any mention of sebaceous glands in the tongue, and because of the rarity of this condition, we wish to report such a case.

REPORT OF CASE

M. K., a 54-year-old, unmarried, white woman, registered at the Skin and Cancer Unit of the New York University-Bellevue Medical Center on Sept. 8, 1951, complaining of a growth on the dorsal surface of the tongue, which she had first noticed two months previously. Inspection revealed a dome-shaped nodule about 2 mm. in diameter located near the junction of the middle and posterior thirds of the tongue. There were no symptoms. On the same site a biopsy was performed under procaine anesthesia, with a punch so as to include the whole of the lesion as far as it could be judged clinically to extend.

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The case included in this paper was submitted in the form of a thesis by Dr. Alvo A. Guiducci to the faculty of the New York University Post-Graduate Medical School in partial fulfillment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

* References 1 to 6.

† References 7 to 12.

‡ References 13 to 15.

§ References 16 and 17.

|| References 19 to 23.

¶ References 24 to 28.

Because of the unusual nature of the histologic findings, all other material submitted at that time to the laboratory was carefully rechecked in order to obviate any mistake of identity. There were no other specimens of sebaceous gland possibilities in the batch.

Microscopic Features.—To each side there was edematous epithelium which was typically mucosal, whereas to the center it more closely resembled epidermis (Fig. 1). The basal margin

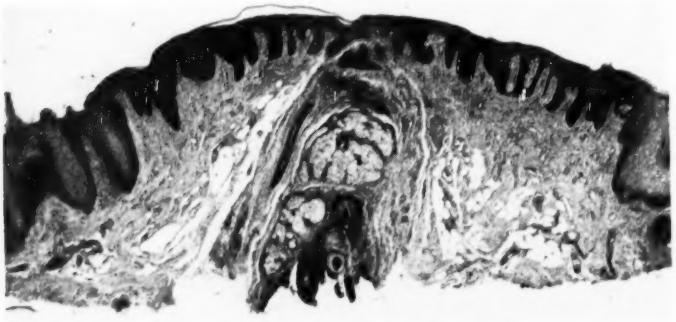

Fig. 1.—Photomicrograph showing sebaceous glands in the tongue; hematoxylin and eosin; × 22.

Fig. 2.—Photomicrograph showing sebaceous glands and structures resembling hair follicles; hematoxylin and eosin; × 88.

Fig. 3.—Photomicrograph of second biopsy specimen showing a tube entering into a rete peg; hematoxylin and eosin; × 46.

was intact throughout. The rete pegs toward the sides were long; some were thick; others were very narrow, and some were fused. The corium showed considerable round cell and fibroblastic reaction, which was largely limited to the papillary and subpapillary zones. The vessels were dilated and found in the large numbers normal for tongue tissue. The mesial side of the section

showed an acanthotic, irregularly branched, but well-marginated epithelial proliferation connected with the surface epithelium. Deep to this, but as far as we could make out not connected with it, there was a tube ending blindly near the surface, and again in the depth, which was lined by a few layers of epithelial cells and which showed a well-formed lumen through the greater part of its length. It ran a rather straight course downwards and slightly diagonally. In the obtuse angle between the structure and the surface epithelium, there were two well-defined sebaceous glands, each one composed of six or seven lobules. The germinative as well as the secreting cells appeared normal and mature. Between the two lobules there was an elongated, irregularly shaped island of epithelial cells, within which there were two spaces (Fig. 2). The lower one was lined by granular cells and contained some partly laminated, eosinophilic material. Prickles could be recognized between some of the lower spaces. Attached to the side of the lower part of this epithelial island, there were two buds composed of "basal" cells. Although no hair could be recognized, the whole structure closely resembled and probably was formed from two distorted follicles.

The patient was called for a check-up and returned to the clinic on March 12, 1952. At the site of the previous biopsy, a slightly elevated papule with an irregular knobby surface was discernible. A larger biopsy was performed to include a greater amount of tissue at the same site. The histologic features of the second specimen were as follows (Fig. 3): There was a very acanthotic, highly irregular, and edematous epithelium, which showed proliferation into the corium and reached the depth of the section; however, the basal margin was intact, and no abnormal cells were seen. A horny layer was present over most of the section, and it showed some parakeratosis. The granular layer was absent except in a few small areas, one of them notably in relation to the structure we shall soon describe. There was a tube running down from the tip of a rete peg to just above the depth of the section. In the lowest part it appeared in cross section, and so the tube was slightly tortuous. In serial section this proved to have a lumen through the greater part of its length, but it ended blindly in the depth as far as we could judge. Its upper end terminated in the epidermis above the rete peg into which it entered, being, however, completely sealed by the upper epithelial layers again to end blindly. Three or four layers of granular cells were seen superjacent to this area. The tube was lined by two and in some places three layers of cells, and in the deeper parts a few desquamated epithelial cells were found in its lumen. The corium showed a widely scattered but banal inflammatory reaction subjacent to the whole acanthotic surface epithelium.

COMMENT

The following suggestions are offered in an attempt to explain embryologically the occurrence of sebaceous glands in the tongue in our case, which is, as far as we know, unique.

The tongue is derived from the first, second, and third branchial arches.[29] The dividing line is marked throughout life by the terminal sulcus in the area of the circumvallate papillae. The body and apex of the tongue originate from three prominences on the oral aspect of the mandibular arch, of which one is situated on each side, and a third unpaired one, called the tuberculum impar, appears somewhat posteriorly between these two. The base of the tongue develops later as a bulge in the middle part of the second and third arches. In the midline, between the derivatives of the first and second arches which contribute to the tongue, the thyroid anlage appears. The thyroid gland anlage begins as a ventral outgrowth of pharyngeal cells about the fourth week of embryonic life. In addition to specialized cells which develop into thyroid epithelium, other elements of pharyngeal mucosa are mechanically incorporated in this anlage. Thus, lymphoid tissue as well as squamous or ciliated epithelium may be found along the course taken by the developing anlage.[30] The above sequence of events makes it conceivable that, during the process of fusion

of the first and second branchial arches to form the tongue, pharyngeal mucosal elements, carrying with them pilosebaceous primordia and sweat apparatus, can be nipped off and incorporated in the lingual tissue.

The formation of the ductus lingualis is usually discussed in connection with the anlage of the thyroid. There is some evidence to indicate that there is no direct relationship between the lingual duct and the thyroglossal strand.[31] Although the foramen cecum in the tongue is usually referred to as the post-natal landmark of the origin of the thyroid, it would appear more correct to designate it as the point of union of the paired buds which form the base of the tongue. If this be true, the foramen cecum marks the pharyngeal opening of the ductus lingualis. Jarvis[32] claims that the early belief that there is, at some developmental stage, a patent lumen in the cylinder of thyroid epithelium (thyroglossal duct) is not true, but that, when it persists, it is only an epithelial strand.

The tubular structures observed and described in our case might represent epithelial elements of the lingual duct rather than remnants of the thyroglossal strand. It is possible that the thyroid anlage in its descent can carry elements of pharyngeal mucosal tissue with it downward, and the tongue which develops later incorporates this tissue in its substance. However, we could observe no lymphoid tissue in the vicinity of the tubular structures, such as is usually found associated with vestigial thyroglossal ducts. No observers have recorded the existence of sebaceous glands associated with thyroglossal tract abnormalities.#

Neither of these two possible origins, i. e., that from the thyroglossal duct and that from the ductus lingualis, would satisfactorily explain the presence of two tubular structures found, one in the first biopsy specimen and a second on reexcision. It would be difficult to conceive their both being parts of one and the same tube. In view of the presence of what must be regarded as two follicular structures, the two tubes are in all probability sweat ducts, either "apocrine" in type, and therefore understandably associated with the pilosebaceous anomaly, though no connection was seen between the tubes and the follicular elements, or eccrine in origin, and therefore understandably entering in rete pegs. Combinations of abnormalities are teratologically not uncommon. Neither of the biopsies was deep, so that we cannot exclude the possibility of the presence of eccrine or aprocrine glands in the deeper tissue, but we, of course, lack the supportive evidence that their presence could have given.

However, the suggestion of the sweat duct nature of the tubes is the one we think most acceptable. Although all theories offered lack complete substantiation, the most plausible explanation of our anomalous case is that of ectodermal sequestration into the lingual tissue during embryonal development.

SUMMARY AND CONCLUSIONS

A unique case of sebaceous glands, follicles, and sweat ducts in the tongue is reported. It is believed that this condition was the result of ectodermal sequestration into the lingual tissue during embryonal development.

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ALLERGIC CONFIRMATION THAT SOME CASES OF ERYTHEMA ANNULARE CENTRIFUGUM ARE DERMATOPHYTIDS

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IN A PREVIOUS article it was stated that some cases of erythema annulare centrifugum are dermatophytids.[1] This was based on the fact that several cases of this disease were found to fulfill the minimal basic criteria for the diagnosis of a dermatophytid. In addition, in two of these cases, erythema annulare centrifugum was reproduced and abolished by the experimental production and eradication of tinea pedis.

In 1930, Epstein and Grünmandel [2] presented a definitive work on the local immunoallergic changes occurring in tinea circinata. In both experimental and spontaneous human tinea circinata, they produced a cruciform superinfection through the center of the annular lesions and demonstrated by this method that local immunity occurred not only in the center of the resolving infection, but also in a zone around the fungous focus. These changes were demonstrable only during a specific phase of the disease. It is likely that this corresponds to the "clearing period" delineated by DeLamater and Benham [3] in their experimental studies with the dermatophytes in guinea pigs.

Epstein and Grünmandel [2] in a similar manner studied the response to trichophytin, and their results may be summarized as follows:

1. Anergy was noted in the center of the annular lesions of tinea circinata, whereas an inflammatory reaction occurred beyond the fungous focus.

2. This local anergy to trichophytin was specific in that it was not present with tuberculin. The tuberculin response corresponded to the general tuberculin allergy, and was independent of the local allergy.

3. Although the allergic response to trichophytin in the skin adjacent to tinea circinata was usually consistent with the generalized allergic response, this was not an invariable finding.

In DeLamater's [4] animal experiments the papular response to trichophytin was of longer duration in noninfected areas than at the site of previous lesions.

Hopkins * emphasized that the above observations were important in explaining the morphology of annular dermatophytoses and the spontaneous resolution of some of these lesions and could be of etiologic value in the study of anergy in annular allergic skin diseases.

All of these investigators agree to the specificity of these immunoallergic reactions. Therefore, a method was available to offer further allergic confirmation that some cases of erythema annulare centrifugum are dermatophytids. Initially, patch

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* Hopkins, J. G.: Personal communications and lectures given at Columbia Medical Center.

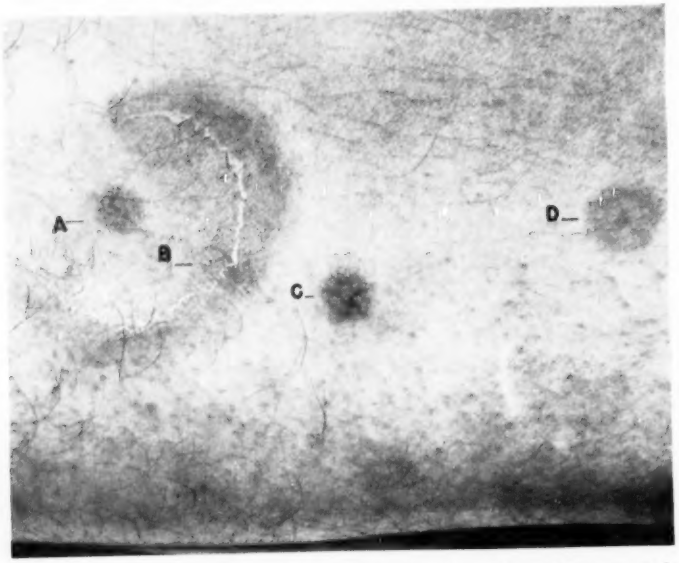

Fig. 1.—Results four days after injecting trichophytin (*A*) within, (*B*) at the inflammatory border, and (*C*) beyond a semiannular lesion of erythema annulare centrifugum. *D* is a spontaneous lesion of erythema annulare centrifugum.

Fig. 2.—Same as Figure 1, but taken seven days after the injection of trichophytin. Note that the trichophytin reaction at *C* mimics the spontaneous lesion of erythema annulare centrifugum at *D*, whereas the skin test site at *A* has faded.

tests with trichophytin were performed through and beyond the lesions of erythema annulare centrifugum.† However, it was discovered that more precise morphologic allergic changes could be demonstrated by injecting trichophytin intradermally both within and adjacent to the lesions of erythema annulare centrifugum.

REPORT OF A CASE

W. H., a 28-year-old man, had a dermatitis of the thighs for six years. It was characterized by the occurrence of erythematous, edematous papules which cleared in the center while enlarging peripherally to produce large semiannular, annular, and gyrate lesions. There was desquamation on the inner aspect of the elevated borders. The lesions were asymptomatic and evolved to the annular configurations during the warm months of the year. During the winter, only a few erythematous, edematous papules appeared on the thighs.

A diagnosis of erythema annulare centrifugum type of dermatophytid was made. This was based on the fulfillment of the minimal basic criteria for the diagnosis of a dermatophytid. Trichophyton mentagrophytes was isolated, both from a vesicular tinea pedis and from a superficial onychomycosis. The trichophytin skin test showed a typical papular tuberculin type of reaction at 48 hours. This papule then cleared centrally while enlarging peripherally to produce a miniature lesion of erythema annulare centrifugum at one week.[1] Biopsy showed a focal infiltrate of monocytes and spongiosis.

During the winter months the annular lesions were deliberately precipitated by the production of tinea pedis through the wearing of heavy stockings, rubber-soled shoes, and cessation of foot hygiene. When active daily antifungal foot care was reintroduced, the lesions disappeared in about two weeks.

METHOD

Trichophytin, 1:30 (Lederle), was injected intradermally, 0.1 cc. within the center of a semiannular lesion, 0.1 cc. at the inflammatory border, and 0.1 cc. outside the lesion into previously uninvolved skin. No immediate wheal reaction at 15 minutes or edematous response at six hours * was noted at these three sites. At 48 hours, all three sites showed a papular tuberculin type of response of equal degree, except that there was some masking of the trichophytin response located at the inflammatory border. By four days, the injected site at the inflammatory border was only faintly discernible, whereas the trichophytin reaction was positive and more pronounced at the test area outside the semiannular lesion than at the one located within its center (Fig. 1). By one week the trichophytin skin test within the lesion was represented by a dull erythematous macule, while the trichophytin skin test outside the lesion showed a 1.5 cm. papule with central clearing. It mimicked an adjacent spontaneous erythema annulare centrifugum lesion both in its morphology and in its evolution (Fig. 2).

Controls receiving PPD, 0.025 mg., and oidiomycin, 1,000 protein nitrogen units per cubic centimeter, given intradermally, produced the typical tuberculin type of responses, showing the same degree of evolution and involution, both inside and outside the lesions. At no time did these skin tests mimic erythema annulare centrifugum.

COMMENT

One of the most important diagnostic features of this dermatophytid is its allergic reaction to trichophytin. A positive trichophytin skin test must be present to make a diagnosis of a dermatophytid, and the response to trichophytin must be of the same clinical and histopathologic appearance as the type of dermatophytid present, with

† Originally suggested by Dr. Adolph Rostenberg, Jr.

rare exceptions. For example, if the dermatophytid is urticarial with or without associated asthma and hay fever, the immediate wheal reaction should appear in 15 minutes. In eczematous dermatophytids of the hands, a tuberculin type of reaction is found. With the erythema annulare centrifugum type of dermatophytids, the tuberculin reaction appears at 48 hours and, instead of fading, enlarges peripherally while clearing in the center to produce at one week or more a miniature lesion of erythema annulare centrifugum. This can best be demonstrated in the regions of the body where the disease occurs in a given patient. An exception to this is found in those areas where the skin lesions have recently involuted. Here only the tuberculin type of reaction is found. These local altered allergic manifestations must signify a specific etiologic factor, which in this case is the dermatophytic antigen.

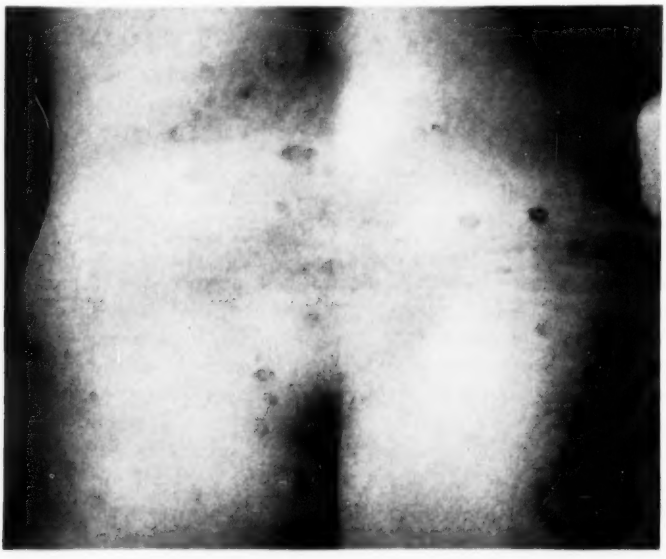

Fig. 3.—Small lesions of erythema annulare centrifugum located over lower back and buttocks.

This central immunoallergic alteration is not the same as the nonspecific intermediate zone.[6] In fact, no "free zone" was found around the lesions of erythema annulare centrifugum.

The milder forms of erythema annulare centrifugum are commoner than is stated in the literature. The lesions are asymptomatic and usually located on the covered parts of the body. Thus, a patient does not consult a doctor primarily for this dermatologic disease. An example of the milder forms of erythema annulare centrifugum is shown in Figure 3. These small annular lesions had been present for three years. On continuous treatment of the superficial onychomycosis and tinea pedis, the lesions disappeared within three weeks, and there has been no recurrence of the dermatitis.

Since the allergic response to a small amount of trichophytin is extreme and of long duration, it is imperative in treatment that daily antifungal foot care be carried

out. Superficial onychomycosis produced by T. mentagrophytes is invariably present and requires treatment by daily use of a nail brush followed by iodine tincture U. S. P.

Not all cases of erythema annulare centrifugum are dermatophytids. However, it is believed that nothing is to be gained by extending the nomenclature of this clinical entity because of variations in morphology.[7] More basic knowledge can be derived by designating these cases under the one name of erythema annulare centrifugum and then by investigating the specific causative antigen, whether it be fungal, bacterial, viral, parasitic, or tumorous.

SUMMARY AND CONCLUSIONS

Some cases of erythema annulare centrifugum are dermatophytids. Allergic confirmation is based on the finding that one week after trichophytin was injected both within and outside a lesion of erythema annulare centrifugum, the inner site was represented by a fading macule, whereas the trichophytin test outside the lesion had enlarged to produce a miniature replica of erythema annulare centrifugum.

It is stressed that the milder forms of erythema annulare centrifugum are commoner than is stated in the literature. For successful treatment, it is necessary to carry out continuous daily antifungal foot care of both the skin and toenails.

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Clinical Notes, New Instruments and Techniques

HYDROCORTISONE IN THERAPY OF CUTANEOUS DISEASE

Preliminary Report

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AND
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Excellent results of hydrocortisone ointment in the treatment of diseases of the skin have been reported by Alexander, Rein, Robinson, Sidi, Sulzberger, and Witten.*

Since the spring of 1953, we have given hydrocortisone ointment a therapeutic trial in patients admitted to Rudolph Bergh's Hospital. In most cases we employed a hydrocortisone alcohol ointment prepared in the pharmacy of the Municipal Hospital, Copenhagen; in others we used Merck's original ointment, and in still others, a preparation supplied through the courtesy of Leo Pharmaceutical Factory, Copenhagen. As a rule, the ointments employed contained 1% hydrocortisone. Experiments with lower concentrations failed to produce satisfactory results. In most cases, concentrations of 0.5 or 0.1% did not even prove capable of maintaining the effect obtained with an ointment of the 1% concentration, which seems clearly to mark the threshold of effectiveness of the preparations available. Various ointment bases have been tried, and at present we are using glyceryl monooleate 2.5 parts, white petrolatum 42.5 parts, wool fat 5 parts, citrate buffer solution pH 5 q. s. ad 100.

As a matter of fact, therapeutic studies with ointments are not easily evaluated. However, the following measures were instituted to provide some controls:

1. In the case of anal eczema, the favorable results were independent of the ointment base, which would appear to rule out petrolatum, for instance, as the responsible factor.

2. Lowering the percentage of hydrocortisone in the ointment or therapy with the ointment base alone produced relapses in a number of patients. These patients responded favorably to additional therapy with 1% hydrocortisone ointment.

3. In patients presenting multiple lesions, some of the affected areas of the skin were treated with hydrocortisone ointment, others with ointment base or other ointments for the purpose of obtaining comparative data.

4. In other cases, the ointment base was employed first alone and subsequently with the addition of 1% hydrocortisone.

RESULTS OF THERAPY

Anogenital Eczema.—The group treated contained 25 patients. Follow-up data are available on all except one. No effect was noticed in 5 patients; in the remaining 19 the response was very good. Itching ceased after a few days of therapy, whereupon there was slow regression of the lichenification, and even in the most severe cases the skin was smooth after one or two months of therapy.

The period of observation is too short to permit definite conclusions as to the duration of the effect, but the majority of our patients would appear to require continuation of therapy for many months, since almost all of them showed signs of relapse when withdrawal of medication was attempted. In view of the fact that several of the patients have had symptoms for from 10 to 15 years and have been refractory to the dermatologic methods generally employed, we feel that even though these chronic cases call for treatment over a very long period, the use of hydrocortisone ointment offers definite improvement in that it is capable of producing freedom from symptoms in these distressed patients.

From Rudolph Bergh's Hospital (Director: Dr. Kristjansen).

* References 1 to 7.

Circumscribed Neurodermatitis.—Seventeen patients with this disease were treated, 15 of whom showed excellent results. There was immediate cessation of itching, followed by a gradual regression of lichenification. As in the case of the group with anal eczema, it is too early to assess the duration of the good results obtained, since most of the patients still require therapy. However, one patient with neurodermatitis of 10 years' standing has been able to do without treatment for a month without experiencing relapse, and two others need only apply the ointment "occasionally," at intervals of several days. Neurodermatitis and anal eczema would thus appear to be the chief indications for the use of hydrocortisone in ointment form.

Atopic Dermatitis.—Our studies have included 38 children and 13 adults with atopic dermatitis.

The period of observation is too short to permit long-term evaluation of results, but in 21 children and 8 adults the effect was favorable. Complete involution, however, is rarely seen.

Eczema.—Hydrocortisone was given a trial in four patients presenting established evidence of allergic eczema. One who was hypersensitive to turpentine showed no improvement, whereas the remaining three became largely symptom-free within a few days.

It was interesting to note the promptness with which freedom from symptoms was produced in three patients with nummular eczema of long standing. In one case, healing took place almost within a matter of hours, and a relapse occurred just as promptly on transition to therapy with the ointment base alone.

Besides the cases already mentioned, this group contained 15 patients with different types of eczema. There was no effect in four, and a questionable effect in two; in one an eczematous eruption on the hand lost its lichenification while some eczematous changes persisted. Excellent results were obtained in the remaining eight cases, i. e., auricular and periocular eczemas refractory to all previous therapy.

Here too, it is too early to determine the duration of results, but there is no doubt that hydrocortisone ointment has produced a complete change in the well-being of these patients. It should be stressed that the treatment is purely symptomatic and very expensive; therefore discretion should be exercised in the selection of cases.

Other Cutaneous Diseases.—Only limited numbers of patients with other cutaneous diseases have been treated so far. Hydrocortisone proved ineffectual in chronic discoid lupus erythematosus (six patients), pemphigus vulgaris (one patient), pemphigus vegetans (one patient), discoid psoriasis (three patients), pustular bacterids (two patients), and lichen planus (two patients). One patient with hypertrophic lichen planus admitted that there had been relief of itching, but complained that hydrocortisone had failed to produce disappearance of the lesions.

COMPLICATIONS

Some of the aforementioned authors have carried out examinations to determine whether hydrocortisone ointment is likely to cause complications in the form of a systemic effect. Their results must be regarded as having established evidence that the amounts of hydrocortisone absorbed by the skin from the ointments employed are so small that the possibility of a systemic action is ruled out.

It is a well-known fact that corticotropin therapy produces a lowered resistance of the organism to infections. There can hardly be any doubt that hydrocortisone ointment exerts a similar effect in the region to which it is applied. We have noticed this especially in patients with atopic dermatitis or seborrheic dermatitis who suddenly developed impetiginization during an otherwise successful course of therapy. In other skin diseases, we found no definite evidence of this side-effect, but discretionary use of the ointment is surely recommendable in mycotic or bacterially infected cutaneous lesions.

SUMMARY

A presentation is made of the preliminary results obtained in the treatment of various cutaneous diseases with an ointment containing 1% hydrocortisone. The immediate results are very promising in diseases like anal eczema, circumscribed neurodermatitis, and various lichenified chronic eczemas, but the period of observation is too short to permit long-term evaluation of results.

An excellent symptomatic response is seen in most cases of atopic dermatitis, but few patients become symptom-free.

Hydrocortisone appears without any effect in lupus erythematosus, pemphigus vulgaris, pemphigus vegetans, psoriasis, pustular bacterids, and lichen planus.

Complications of a systemic nature are unlikely, but, especially in the case of atopic dermatitis, a marked reduction in local resistance to infections is seen.

It is concluded that in a number of cutaneous diseases 1% hydrocortisone ointment is capable of producing an effect comparable to that of systemic corticotropin therapy.

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DERMATITIS HERPETIFORMIS

Note Regarding Treatment

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During 1952 I treated a 54-year-old man who presented an extensive and very pruriginous dermatitis herpetiformis which was of six years' duration. It involved the scalp, the shoulders, the buttocks, the arms, and the legs.

In spite of the recognized form of treatment, which included autohemotherapy, sulfapyridine, superficial x-ray radiations, and topical mentholized lotion applications, no improvement was noted. (Elsewhere previously he was given arsenic by mouth, both in the form of potassium arsenite [Fowler's solution] and the Asiatic pill [containing arsenous acid and black pepper] to the point of toleration, without relief.)

When 12 weeks of the above treatment produced no significant change, I stopped it. Everything was discontinued.

The patient was vaccinated with smallpox vaccine. The vaccination caused a severe local and a general reaction, and it was followed by a dramatic amelioration of the itching and also of the objective symptoms.

At the end of two weeks the vaccination was repeated. A minor take was observed and further, though less distinct, improvement was registered.

The vaccination was repeated at two-week intervals for 14 consecutive vaccinations. Some were followed by attenuated takes, while in some instances there was no evidence of a local reaction.

After six vaccinations the symptoms seemed to remain stationary. The scalp and the legs were still involved and moderately itchy. At this time he was instructed to resume the medication with sulfapyridine, 7½ grains (485 mg.) t. i. d. Slowly most of the symptoms subsided.

Occasionally there occur episodes of itching and minor herpetiform eruptions on the scalp and on the legs, which are easily kept under control with the ingestion of sulfapyridine.

During 1953 I treated a 60-year-old man, who presented a less dynamic dermatitis herpetiformis, with the addition of smallpox vaccination every 14 days to the usual sulfapyridine and topical treatment. The first vaccination caused a severe local and general reaction, while the subsequent ones were followed by only occasional and very mild takes.

I obtained a distinct impression that the addition of vaccination with smallpox vaccine was of appreciable benefit in the second patient.

I therefore recommend the application of this treatment in any of the recalcitrant forms of dermatitis herpetiformis, which unfortunately is common.

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USE OF VITAMIN C IN ACNE VULGARIS

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The use of vitamin A in the treatment of acne vulgaris has been the object of much study,* and, while vitamin A has been given to many patients with acne over the past several years, it seems to help only a few of them. Frazier and co-workers[3] have shown that, in some acne cases, lack of vitamin A causes a hyperkeratinization of the hair follicles, and an accumulation of this keratin, with the secretions of the glands, is a factor in the plugging of the pores. Upon administering vitamin A, the keratin of the hair follicles returns to normal in certain cases, with the result that the plugging of the pores is much more infrequent. Inasmuch as vitamin A helps only a few cases, however, and since vitamin C is also known to play an important part in normal keratinization, as well as in combating infections and infectious diseases,[6] it was deemed advisable to study the role of vitamin C and citrus juices in a series of acne cases.

Other considerations that seemed to indicate that a study such as this should be undertaken were the following:

First, in a recent report made by the British Medical Research Council as to an experimental study of vitamin-C deprivation,[7] it was stated that "five of the volunteers, deprived of Vitamin C, showed a very pronounced exacerbation of the acne present in a mild form at the start of the experiment. The papules became more numerous after about 22 weeks; they increased in size and later became bright red and eventually haemorrhagic."

Secondly, Sulzberger and Wolf state in their book[8] that lack of vitamin C can cause hyperkeratosis, and they urge that vitamin C be given in cases where its deficiency is noted.

Therefore, 60 patients with acne were given an 8-oz. glass of citrus juice twice daily and ascorbic acid in dose of 3 gm. a day, their condition being followed over a period of approximately four months. This is a relatively short period for any study of acne, for most previous studies have been from six to nine months or even longer, but it was my conviction that, if vitamin C was to help any cases, improvement should be noted in at least four months.

Of 53 patients who returned for adequate treatment, 43 showed improvement; 10 failed to show improvement, and the other 7 did not return for follow-up. The most interesting group, and those from whom the most could be learned were either those whom I had observed under my care for protracted periods prior to the commencement of this study, or patients who had had extensive treatment elsewhere and who showed dramatic improvement without any change in their regimen except the addition of vitamin C and citrus juices. All of the patients were given a diet free of chocolate, cocoa, nuts, and peanut butter, were told to clean their skin three times a day, and were given sulfurated potash lotion (lotio alba) to apply at night. The patients were graded from 1+ to 4+ as regards papules, pustules, and comedones, 1+ being mild, and 4+ being severe.

Of the 43 patients who did improve, 15 were those who had been treated for anywhere from eight months to seven years by me without being cured, prior to the administration of the vitamin C. In at least these 15 cases, the administration of vitamin C seemed to improve them more than any other mode of treatment that they had received.

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* References 1 to 4.

CONCLUSION

Of 53 patients who were treated for acne vulgaris with routine therapy but with vitamin C and citrus juices added, 43 improved in a period of four months; 10 did not improve. Of the 43 patients, 15 had previously been treated without marked improvement, but showed dramatic improvement shortly after the administration of vitamin C and citrus juices without change in the previous method of treatment.

This study seems to substantiate the findings of the British Medical Research Council in that vitamin C and citrus juices play an important part in certain cases of acne.

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Correspondence

SIMPLIFIED NOMENCLATURE FOR NEVI

To the Editor:—I read with some surprise Dr. Arnold's (Arnold, H. L., Jr.: Simplified Nomenclature for Nevi, Correspondence, A. M. A. Arch. Dermat. & Syph. **69**:624 [May] 1954) "protest against the perpetuation of the currently accepted confusing and unnecessarily complex terminology used to designate varieties of the common benign mole or cellular nevus, and to propose a simplified nomenclature."

In the first place, his listing of "present terms" in my opinion was an outmoded one and not currently accepted. His suggested names of "growing nevus" and "mature nevus" depend on supposition rather than on proof. Of course nevi do have growing periods and become mature, but this growing period varies tremendously. In other words an infant might have a mature nevus whereas an adult might and frequently does present a growing nevus. While I was not at all convinced that the classification which I proposed many years ago (Traub, E. F., and Keil, H.: The "Common Mole": Its Clinicopathologic Relations and the Question of Malignant Degeneration, Arch. Dermat. & Syph. **41**:214-249 [Feb.] 1940) and which I list herewith,

1. Intraepidermal nevus
2. Intradermal nevus
3. Junction or borderline nevus
4. Combination type nevus
5. Blue nevus

is one that can be called final or one that should be generally accepted without modification, nevertheless, it was the first attempt to take chaos out of a very complex subject. It also made possible the prediction of prognosis of a given nevus which heretofore to my knowledge had not even been attempted. The anatomy of the skin is not too complicated for any physician to understand; even nondermatologists know that we have an epidermis and cutis or derma. Therefore, I do not believe that the classification that I proposed should be beyond the intelligence of the average physician to grasp. The terms are clear and one can easily understand that any intradermal nevus is one lying within the derma or cutis and that the junction nevus is one marking the junction or border between the epidermis and cutis. A mixed nevus is exactly that —one in which a blue nevus and a junction or intradermal nevus are found in the same section. It was my thought that these terms would not sound complicating or complex and that the classification would clarify prognosis because we know exactly what one may expect from a nevus fitting into each category. This I believe has been accomplished, because we are now positive that an intradermal nevus is and always remains a benign nevus, that some junction nevi may terminate as malignant melanomas, and so on. Heretofore it had only been stated in medical histories that the patient had had a "mole" that became malignant. This was the type of language that most dermatologists deplored because it sounded too much like saying that the patient had a "papilloma," another entirely meaningless term.

All junction nevi do not continue to grow beyond a certain point. They reach a fixed point exactly the same way that intradermal nevi remain fixed after reaching a certain point in their growth. Only the junction nevi that continue their unrestricted growth become malignant lesions and they are fortunately "few and far between." Thus all nevi are "growing" at some stage and "mature" at another point. It can readily be seen that this can be carried to absurdity, and that if we wish to lose all the information that we have laboriously gleaned in the study of these congenital anomalies, the classification proposed by Dr. Arnold can go far toward destroying this valuable information. I do not believe that all malignant lesions should simply be classified as malignant without stating what they are, from what tissue they arise, or what their potentialities might be.

Eugene F. Traub, M.D.
140 E. 54th St.
New York

To the Editor.—My recent note on the nomenclature of cellular nevi was intentionally brief; so brief, I fear, that it seemed to imply a lack of respect for Dr. Traub's important contribution to our understanding of these lesions. I vividly recall the first case of growing nevi (intraepidermal, junction, or compound, depending on the plane of the section) I ever encountered, while I was in training, in 1938. It was regarded as so remarkable and puzzling as to be worth reporting, and was reported (Arnold, H. L., Jr.: Multiple Pigmented Nevi: Report of a Case, ARCH. DERMAT. & SYPH. **40**:386-389 [Sept.] 1939). Today this case would be regarded—thanks to Dr. Traub's publications on the classification of these lesions—as utterly commonplace.

A morphologic classification is a valuable advance, in that it defines terms and permits communication of ideas. If a biologic classification can develop out of it, however (*vide* Hansen's classification of leprosy, and Michelson's classification of cutaneous tuberculosis), a further advantage has been gained.

I admit that supposition, without proof, is all that can be offered to support the terms "growing" and "mature." I submit, however, that Dr. Traub's Types 1, 3, and 4—which show the "junction" phenomenon (*Absonderung* and *Abtropfung*)—all have in common the characteristic of activity, or growth, and the potentiality (remote though it is) for malignant change, and can therefore very well be regarded as a single variety of cellular nevus. His Type 2, the intradermal nevus, stands (with its presumed though unproved incapacity for malignant change) in sharp contrast to the other three.

Moreover, though I agree with Dr. Traub that it is not unreasonable to expect physicians generally to understand what is meant by "intraepidermal," "intradermal," "junction," and "combination" or "compound," as applied to cellular nevi, I feel sure they haven't done so and I doubt if they ever will. Many general pathologists are already using them in a slightly different sense from that proposed originally. I don't insist that "growing" and "mature" are the best terms. Perhaps "junction" and "mature" would be better. I do feel, however, despite my sincere and profound respect for Dr. Traub's views, that the classification of these lesions should be binary, and that the terms used should be more nearly self-explanatory, in order for the general pathologist, the surgeon, and the family physician to know what we are talking about.

HARRY L. ARNOLD, JR., M.D.
Straub Clinic
Honolulu, T. H.

EFFECT OF TOPICAL AGENTS ON PLANTAR SWEATING

To the Editor:—In their interesting paper on this subject published in the A. M. A. ARCHIVES OF DERMATOLOGY AD SYPHILOLOGY (**69**:713 [June] 1954), Drs. Shelley, Laskas and Satanove conclude that "no simple topical method is now available for appreciably inhibiting the normal action of the plantar sweat gland" but mention that a single application of formalin appreciably reduced plantar sweating for more than one week in 17 of 50 normal subjects.

For about 20 years, I have had entirely successful results in hyperhidrosis of the soles with the use of formalin applied in the following way. Undiluted, the formalin is painted over the weight-bearing surface of the foot, by means of a cotton swab, care being taken not to apply it to the interdigital areas. The painting is repeated once daily for three or even, in severe cases, four days, and repeated in four weeks if necessary. The applications should be made by the physician unless the patient is particularly intelligent.

I have employed this simple treatment in hundreds of cases both in Britain and in the Mediterranean area; only one patient developed any reaction, in the form of a mild contact dermatitis which healed in a week.

G. A. GRANT PETERKIN, M.D., Edinburgh.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Nathan Sobel, M.D., *President*

Henry Silver, M.D., *Secretary*

Nov. 19, 1953

Reticulum Cell Sarcoma with Cryoglobulinemia. Presented by Dr. Frances Pascher.

DISCUSSION

Dr. Frances Pascher: In this 33-year-old woman the striking features were "cold urticaria" for three successive winters, followed by purpura aggravated by exposure to cold, and elicited by the application of ice packs to the skin; a purpuric eruption most marked on the legs, closely resembling the so-called "pigmented lichenoid eruptions of the lower extremities"; and the finding of cryoglobulins in the blood. The patient died 20 months after the second presentation before this Society. Hypertension, albuminuria, progressive hepatosplenomegaly, and retinitis were noted before death. The essential findings on autopsy were a reticulum-cell sarcoma of the lungs, liver, spleen, and lymph nodes, and a periarteritis nodosa of the heart, aorta, and the abdominal viscera.

Dr. Irwin R. Cohen, who has made a search of the literature, has found only one other case on record of reticulum-cell sarcoma associated with cryoglobulinemia. Most of the cases of cryoglobulinemia reported to date have been linked with multiple myeloma or kala-azar.

An abstract of the case presented before this evening can be found in the *Transactions of the Section of Dermatology and Syphilology, New York Academy of Medicine, May 6, 1952* (**67**:429-430, 1953).

Alopecia Universalis Treated with Oral Cortisone. Presented by Dr. Victor H. Witten and Dr. Marion B. Sulzberger.

S. L., a 42-year-old white woman, was first seen in private practice on March 30, 1951. One year before she noted sudden onset of loss of hair from scalp, which rapidly extended to the extremities, trunk, and lastly the eyelashes.

Previous therapy, including phenol paintings, grenz radiation, vitamins orally and by injection, hormones by injection and topically, sedatives, and the local application of cortisone acetate, failed to produce any changes.

On Jan. 3, 1952, the patient was started on 100 mg. of cortisone acetate orally in divided doses daily. This amount was continued until Oct. 31, 1952, when it was reduced to 75 mg. daily.

On March 27, 1953, the dose was reduced to 50 mg. daily, but it had to be increased again to 75 mg. a day on April 10, because the remaining spots of alopecia were increasing in size and new ones were appearing. By May 14, the patient was taking 150 mg. a day.

On June 2, hydrocortisone, 120 mg. a day, was given in place of cortisone. Since then the dose has been reduced gradually. The current dose is 80 mg. of hydrocortisone a day. The steroid intake was accompanied by a low-salt diet and supplemental potassium in the form of potassium chloride.

Clinical and Laboratory Studies: Weekly checks of blood pressure and weight together with urinalyses have shown no deviations from the expected norm. Determinations of blood sodium, potassium, and glucose have remained within normal limits.

Very recently the patient complained of a feeling of slight depression and weakness. A thorough physical examination, including laboratory work-up, revealed some impairment of adrenocortical function, as follows: decrease in minerocorticoids, as manifested by muscle spasm and weakness, low blood sodium, and high serum potassium; decrease in androgenic steroids, as

manifested by low 17-ketosteroid excretion. Corticosteroid activity (from exogenously administered hydrocortisone) was evidenced by normal glucose and insulin tolerance tests and high 11-oxysteroid excretion.

DISCUSSION

DR. VICTOR H. WITTEN: When we cut the dose of cortisone to 50 mg. a day the patient's hair began to fall out, and on raising the dose her hair began to grow in again. We substituted one 20 mg. tablet of hydrocortisone for one 25 mg. tablet of cortisone. It is difficult to work out the exact comparative effective dose between hydrocortisone and cortisone in this case because of the time lag after decreasing or increasing the dose and the falling out of hair or its regrowth. In rheumatoid arthritis the effectiveness of hydrocortisone as compared to cortisone has been stated to be a ratio of about 1:1.6; thus hydrocortisone is considered about 50% more effective than cortisone, milligram for milligram.

Kaposi's Sarcoma of the Scrotum Treated with Quinacrine (Atabrine). Presented by DR. FREDERICK REISS.

N. P., a 50-year-old white man of Italian extraction, presented on June 22, 1953, eight nodules distributed over the scrotum and pubic area. These lesions, according to the patient, developed within two to three weeks. The nodules ranged in size from that of split-pea to that of a small hazelnut. One of the lesions resembled a pyogenic granuloma, which bled easily.

Microscopic examination of tissue taken from the latter lesion showed the following: The epidermis is flattened. In the mid and upper cutis there is a large circumscribed mass consisting mostly of closely packed, spindle-shaped fibroblasts. Throughout the mass, small hemorrhages and extravasated blood cells can be seen. Surrounding the lesion, the vessels are markedly dilated and are surrounded by a lymphocytic infiltrate. Microscopic diagnosis: Kaposi's sarcoma.

Treatment was instituted on Sept. 7 and consisted of 0.1 gm. of quinacrine t.i.d. for four weeks. Since October the patient has taken 0.1 gm. of quinacrine once daily.

Of the original eight lesions five have disappeared.

DISCUSSION

DR. JOHN GARR: This is a very interesting case. However, I would like to see the results in those very extensive cases of Kaposi's sarcoma involving the lower extremities, particularly the feet, toes, and ankles, with pronounced edema. Quinacrine has been shown to produce regression of the tumors in mice (Cramer, H., and Briomayer, C.: Tumor Diagnosis with Quinacrine [Atabrine], *Munchen. med. Wchnschr.* **94**:1642 [Aug. 15] 1952).

Dr. Sulzberger and I tried quinacrine in a case of infiltrated and tumor stage of mycosis fungoides without any result, but that does not rule out a possibility of benefit in other cases of mycosis fungoides. There may be a relationship between Kaposi's sarcoma and mycosis fungoides insofar as Kaposi's sarcoma, like mycosis fungoides, may be a disease of the reticuloendothelial system. Dörffel (Histogenesis of Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, ARCH. DERMAT. & SYPH. **26**:608-634 [Oct.] 1932) considered Kaposi's sarcoma as a disease of the reticuloendothelial system related to the lymphoma group of diseases.

DR. EARLE W. BRAUER: I should like to ask Dr. Reiss what prompted him to use quinacrine in the first place?

DR. MABEL G. SILVERBERG: This is a very interesting case. In lupus erythematosus the use of quinacrine gives striking results, with blanching appearing in a matter of one to two weeks. It is of interest to note what results have been obtained with this drug.

DR. FREDERICK REISS: This is my first personal experience in which I have observed Kaposi's disease with the unusual onset in the scrotal and pubic area. As a matter of fact, only very few cases have been published with a similar history. The second reason for presenting this case is the therapeutic effect of quinacrine. The rationale in using this drug is twofold. As Dr. Silverberg already pointed out, the drug has an effect upon the cutaneous vessels. Another consideration leading me to use this drug is the possibility that Kaposi's disease may be caused by an infectious agent which may be combatted with quinacrine in a similar way to discoid lupus erythematosus. You are probably familiar with Dr. Ludwik Gross's contribution, in which he proved leukemia developing "spontaneously" in mice is caused by a filtrable agent

(Gross, L.: Biological Properties of Mouse Leukemia Agent, *Cancer* **6**:153, 1953). He also succeeded in transmitting the disease to mice of the C3H line, which are known to be free from the disease. Assuming therefore a virus etiology of leukemia, a similar etiology of Kaposi's disease may be considered. Whether quinacrine had a therapeutic effect, or whether the improvement was a spontaneous remission, can be decided only after further observation.

Tinea Capitis ("Black Dot Ringworm"). Presented by DR. ANDREW G. FRANKS and DR. EMANUEL MUSKATBLIT.

DISCUSSION

DR. EMANUEL MUSKATBLIT: The patient is presented because this form of ringworm is a rarity in New York City. Our cases of tinea capitis are usually caused by fungi of the genus Microsporum, either M. audouini or M. canis (lanosum). Lesions due to these fungi are, as a rule, well-demarcated patches with abundant scaling. The infected hairs are in the form of short broken-off stubs which fluoresce green under Wood's light. Microscopic examination of such hairs shows fungi as a dense mass of small, 2 to 3 μ spores outside the hair. This girl presents an ill-defined area on the top of the scalp, with very little scaling and numerous infected hairs in the form of black dots imbedded in the epidermis and resembling blackheads which do not show any fluorescence under filtered ultraviolet light. Fungi can be seen under the microscope as large, 4 to 5 μ spores closely packed inside the hair, a picture suggesting Trichophyton endothrix. Cultures have been made, and their results will be reported. The patient will probably need roentgen-ray epilation, since cases of tinea capitis due to Trichophyton endothrix are known to be resistant to local medication.

Epidermal Dysplasia in Siblings with Congenital Dislocated Hips. Acrokeratosis Verruciformis (Hopf)? Epidermodysplasia Verruciformis (Lewandowsky and Lutz)? Vulgar and Plane Warts. Presented by DR. MORRIS LEIDER.

Xanthoma Disseminatum (Juvenile) with Some Regression of the Lesions After Two Years. Presented by DR. JOHN GARB.

Pemphigus Vulgaris. Fourth Year of Control with Continuous Corticotropin (ACTH) Therapy. Presented by DR. MORRIS LEIDER.

Acrodermatitis Chronica Atrophicans. Presented by DR. NORMAN B. KANOF and DR. IRWIN I. LUBOWE.

A Case for Diagnosis: Bullous Dermatosis? Presented by DR. NORMAN B. KANOF.

Erythema Induratum (Bazin). Presented by DR. ABRAHAM J. ORFUSS.

Senear-Usher Pemphigus with Features Suggestive of Dermatitis Herpetiformis. Presented by DR. FRANCES Pascher.

Persistent Lesion of the Lower Lip Treated with Resin of Podophyllin. Presented by DR. ALEXANDER A. FISHER.

1. Alopecia Universalis, with Regrowth of Hair. 2. Atopic Dermatitis, In Remission. Presented by DR. ABRAHAM J. ORFUSS.

Herpes Gestationis (RH positive, Type O) Treated with Cortisone and Progesterone. Presented by DR. ALEXANDER A. FISHER.

Pigmented Nevus (Junction Type) of Penis. Presented by DR. JOSEPH L. MORSE.

Erythema Annulare Centrifugum (Darier). Presented by DR. ALEXANDER A. FISHER for DR. MAX WOLF.

Keloid Treated with Hyaluronidase. Presented by DR. FREDERICK REISS.

Darier's Disease. Presented by DR. ALEXANDER A. FISHER.

Case for Diagnosis: Seborrheic Dermatitis? Systemic Lupus Erythematosus? Presented by DR. ALEXANDER A. FISHER.

CHICAGO DERMATOLOGICAL SOCIETY

Samuel J. Zakon, M.D., *President*
Irene Neuhauser, M.D., *Secretary*

Jan. 20, 1954

Calcinosis Cutis. Presented by DR. DAVID OMENS, and (by invitation) DR. HAROLD OMENS and DR. LEONARD HOIT.

DISCUSSION

DR. THEODORE CORNBLEET: Calcinosis is a heterogeneous group, even if we leave out of consideration the secondary variety, as that in scars and consecutive to other morbid processes. The members of the group vary as to prognosis and associated relationships. The localized variety shows surprisingly little tissue change surrounding the depots; blood calcium level is normal,

and there are few or no symptoms. The disseminated variety, as shown by this woman, always involves the skin and occurs in one obviously ill. The prognosis is poor, despite little change in the blood chemistry other than an alteration in the protein fraction, usually a deficient one. The third variety is based on systemic processes such as leukemia, in which calcium is mobilized from bone and shifted and deposited elsewhere. Blood calcium, phosphorus, and phosphatase are deranged. Hyperparathyroidism or excessive vitamin D administration may bring it about, and, unless the process is reversed, the prognosis is poor.

Hyperlipemic Xanthomatosis. Presented by DR. ALLAN L. LORINCZ (by invitation).

History.—The patient, M. V., a 16-month-old white girl, first developed skin lesions eight months ago. These lesions appeared as persistent yellowish papules initially at sites of mosquito bites on the legs. Similar lesions then appeared on both heels and at sites of abrasions. During the past two months additional papules have appeared in showers on the buttocks, knees, and face. The lesions have remained asymptomatic. A few of them have shown tiny areas of central necrosis. Except for these lesions and poor appetite in the past three months, the child has been subjectively well.

Physical Examination.—Examination in addition to the skin lesions revealed a slightly enlarged spleen, a few nodules on the tongue, and a striking creamy appearance of many of the small retinal blood vessels.

Laboratory Findings.—Routine blood counts and urinalysis were normal.

Blood chemical analyses revealed the following per 100 ml.: glucose 87 mg.; nonprotein nitrogen 19.5 mg.; serum lipids 1,885 mg.; serum cholesterol 570 mg.; serum cholesterol esters 475 mg. Glucose tolerance test was slightly elevated but not sufficiently to make a diagnosis of diabetes.

Roentgenograms of the chest, pelvis, skull, and upper and lower extremities have all shown normal conditions. The electroencephalogram was also normal.

Examination of the bone marrow shows a few fat-filled histiocytes.

Histologic examination of a biopsy specimen taken from a lesion on the left calf shows thinning of the epithelium over a dermal papule. Throughout the dermis are numerous connective tissue cells, among which large foam cells predominate. Some multinucleated foam cells are also present.

Investigation of other members of the family for hyperlipemia is currently under way. A four-month-old sibling has grossly lipemic serum.

DISCUSSION

DR. A. C. CURTIS, Ann Arbor, Mich.: I did not see the patient at Cook County Hospital, but I did see the child at the University of Illinois with the hyperlipemic xanthomatosis. Hyperlipemic xanthomatosis produces a clinical picture which is the same as a xanthomatosis of the hypercholesterolemic type. Both are hereditary diseases with different metabolic abnormalities. In a marriage of two people with essential familial hypercholesterolemia, xanthoma tuberosum occurs in 25% of the offspring. The hereditary metabolic defect is the hypercholesterolemia (Wilkinson, C. F.; Hand, E. A., and Fliegelman, M. T.: *Ann. Int. Med.* **29**:671, 1948).

This child presents a different metabolic and genetic problem, which is hyperlipemia. The blood abnormalities of fat metabolism in this patient are more the type one would expect to find in the severe diabetic. Any severe uncontrolled diabetic who develops hyperlipemia and hypercholesterolemia can develop xanthomatous lesions. If such a patient is controlled with insulin, the xanthoma lesions clear. This type may be much more amenable to dietary measures which will control the hyperlipemia than is the hypercholesterolemic type of xanthomatosis.

In biliary cirrhosis, one is dealing with both hyperlipemia and hypercholesterolemia on the basis of liver disease.

DR. CARL W. LAYMON, Minneapolis, Minn.: The patient at Cook County Hospital presents extensive lesions on the palms. Xanthomatous lesions on the palms are seen frequently when the liver is involved.

DR. THEODORE CORNBLEET: When heparin is injected intravenously into a postprandial animal, its turbid blood serum becomes clear. It has been learned that this process depends on a

still incompletely understood complicated factor, one of which is the production of a so-called "clearing factor" mostly in the abdominal viscera. It might be well to try this procedure in the patient with hyperlipemia. I have an idea it would reduce the degree of lipemia temporarily, without altering the ultimate poor prognosis.

DR. STURE JOHNSON, Madison, Wis.: Heparin has been used in a patient of ours with xanthoma tuberosum and hypercholesterolemia. As long as a patient remains on treatment the tumors become smaller and the blood cholesterol lower. Because of hemorrhagic tendencies caused by heparin, the drug has been stopped, with recurrence of abnormalities.

DR. ALLAN L. LORINCZ (by invitation): There are a few points I would like to call attention to. One is the striking appearance of the fundi. Peripherally the retinal vessels have a creamy appearance. This has been described as lipemia retinalis. This child has a younger sister who also has lipemia. Thus we are apparently dealing with a familial idiopathic hyperlipemia. This is a very rare disease in children, with only a few cases reported in the literature. We plan to try heparin therapy in this child. It has been claimed that even subanticoagulant doses of heparin are effective in reducing hyperlipemia.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. JAMES R. WEBSTER and DR. STANLEY HUFF and (by invitation) DR. HAROLD MARKS.

DISCUSSION

DR. ROBERT KIERLAND, Rochester, Minn.: Several years ago Dr. Curtis' department reported a case which had a skin graft in the area of necrobiosis. Has Dr. Curtis had further experience with grafting?

DR. A. C. CURTIS, Ann Arbor, Mich.: The patient referred to still has had no recurrence of the necrobiosis in the grafted area. Other patients have been grafted and reported as having necrobiosis return in the grafted area. I wonder if the grafts in which recurrence took place were split-thickness rather than full-thickness? It seems to me a split-thickness graft would be inadequate for such a deep lesion.

DR. FRANCIS W. LYNCH, St. Paul, Minn.: Many patients with necrobiosis lipoidica diabeticorum have no evident hyperlipemia, and certainly no more hyperlipemia than many other diabetic patients. It has been assumed that in necrobiosis there has been previous vascular damage and probable thrombosis. It is interesting to consider possible relationships between heparin and necrobiosis in comparison with those between heparin and xanthomatosis.

DR. THEODORE CORNBLEET: We can flatten the lesions of multiple xanthomatosis by repeated injections of heparin. The involuting xanthomas undergo interesting histological changes. Such a procedure might work in necrobiosis lipoidica, too. I would be tempted to try it.

Sickle Cell Anemia with Leg Ulcers. Presented by DR. SAMUEL M. BLUEFARB, DR. A. I. GOLDBERG, and DR. H. K. MITCHELL (by invitation).

DISCUSSION

DR. FRANCIS W. LYNCH, St. Paul, Minn.: The ulcers associated with sicklemia have interested many dermatologists and they are difficult to explain. Sicklemia is present in a considerable proportion of the population and is assumed to be present from birth. (In one of these patients it has been recognized for 11 years.) If these ulcers of the leg are caused by injury, as many claim, why do they not occur in childhood, since injury is so frequent then? Apparently the ulceration of sicklemia occurs without reference to presence or absence of anemia. Probably the ulcers result from thrombosis, due to the abnormal shape of the cells or the abnormal isomeric form of hemoglobin which is present. I do not think it is common to see the irregularity and angular margins of the lesion that was present in the male patient. He is moderately disabled by his ulcers, and this affords an excellent opportunity to excise not only the ulcer, but the area around and below it, and to study this tissue by serial sections and by injection and dissection of the vessels, a manner of study which to my knowledge has not been done previously in this disease. A transplant would, of course, be applied to the site of excision.

Papulonecrotic Tuberculids. Presented by Dr. Adolph Rostenberg and (by invitation) Dr. G. Fleming.

History.—The patient is a 33-year-old white man. In 1945 he had a prostatic discharge associated with fatigue, weakness, anorexia. The cause of the prostatic discharge was undetermined. Shortly thereafter active tuberculosis of the apex of the left lung was discovered. The patient was hospitalized in a sanatorium in 1947 and treated with general measures. In April, 1949, he had a thoracoplasty, and after this operation, because of fever, he was treated with streptomycin for three weeks. In November, 1949, the patient was discharged as an inactive tuberculosis case.

He has had hay fever and asthma for many years (ragweed sensitive). In 1950 he started to take injections for this and shortly thereafter developed red, deep-seated, infiltrated papules of face, ears, trunk, and extremities. These papules develop a pustular central core which, when expressed, leaves a small cicatrix. He denies ever having had any scarring lesions except a rare occasional boil or ordinary acne prior to this.

Physical Examination.—Examination was noncontributory except for the left thoracoplasty and skin lesions.

Laboratory Findings.—Complete blood count was normal. The blood chemistries were normal. Culture and smear of prostatic secretion were negative. Gastric washings were negative. Urinalysis—24-hour specimen—was negative. Kahn and Wassermann tests were negative.

X-rays of the chest revealed thoracoplasty of left chest with no evidence of active tuberculosis. Intravenous pyelogram was negative. X-rays of long bones were negative.

Pathologic report (Dr. Szymanski): The histologic section from an early lesion revealed mild acanthosis, a moderate amount of round-celled infiltrate with vascular dilatation in the upper corium, plus mild fibrosis in the region of the hair follicles. A diagnosis of chronic inflammation with fibrosis was made.

The second biopsy specimen from an old lesion revealed an epidermis which had been flattened by a very dense fibrotic reaction throughout the upper two-thirds of the corium. Many blood vessels were seen within this fibrotic zone. A diagnosis of scar or fibrosis was made from this section.

Immunologic studies were as follows: 48-hour intradermal reactions to 1:1,000,000 O.T. +; 48-hour intradermal reactions to 1:100,000 trichophytin +; 48-hour intradermal reactions to 1:100,000 Monilia extract +.

Patch tests: O.T. 1:1000 +; Monilia extract 1:500 ±; 1:100 ±; 1:50 +; trichophytin 1:100 0; 1:50 +.

Animal Inoculations: A 5 mm. punch biopsy of a fresh papule was taken. This was ground under sterile conditions with saline in a homogenizer. Approximately 0.1 cc. of the resulting suspension was inoculated into each of four guinea pigs that had been previously shown to be tuberculin negative. These pigs now manifest a positive tuberculin reaction.

Patch test readings at 120 hours: anterior O.T. 1:1000 +; 1:500 +; 1:100 +; Monilia 1:500 0; 1:100 +; 1:50 +; posterior trichophytin 1:500 0; 1:100 0; 1:50 +.

Dermatitis of the Face. Presented by Dr. Vera H. Leaf.

DISCUSSION OF PRECEDING CASES

Dr. H. E. Michelson, Minneapolis, Minn.: I questioned the first patient (presented by Drs. Wells and Rothman) carefully, and she states she has two children and has been well all her life; that there is not any indication of even the mildest tuberculous infection, and also that the tuberculin test is negative. I think she has the lupoid type of rosacea, and I think it is a very serious thing to diagnose these things as tuberculous on the microscopic finding in the skin section. Tuberculosis is a serious disease, and the diagnosis may have far-reaching effects on the patients' psyche.

The case of Drs. Rostenberg and Fleming I think is a disseminated form of lupus vulgaris, the diagnosis being based on the lesion and on the fact that plaques have formed, and on the duration. I think this is a good case for chemical therapy.

Dr. Frederic T. Becker, Duluth, Minn.: I would like to ask Dr. Rostenberg a question. How specific or diagnostic is this test of injected suspected tuberculous material into a tuberculin-

negative guinea pig? If this pig then becomes tuberculin positive, does this establish a diagnosis of tuberculosis? Is it possible to sensitize the guinea pig to tuberculin by previous tuberculin testing?

DR. ADOLPH ROSTENBERG: You cannot sensitize a guinea pig or any other species to tuberculin with tuberculin. You have to introduce whole organisms either dead or alive. The pigs that developed a positive tuberculin reaction developed it from the material secured at biopsy. The only reasonable conclusion is that there were tubercle bacilli in that material. All four pigs became positive. It is only two weeks since we did that, which is a rather short time to develop a tuberculin sensitivity in a guinea pig. It probably means that there is an active infection in these animals. (Since this discussion was given, a further investigation of these results has cast considerable doubt on their validity.)

I would like to say a few words on the case we presented. I think this man has papulonecrotic tuberculids. He may also have lupus vulgaris. All of us at Illinois wondered about the appearance of the plaque on the arm and whether it could be lupus vulgaris. He, however, has distinctly necrotic lesions on the arms, with central plugs, none of which conform to the morphological criteria of lupus vulgaris, but do fit, of course, the diagnosis of papulonecrotic tuberculid. As Dr. Michelson knows, papulonecrotic tuberculids and lupus vulgaris can coexist. I agree with Dr. Michelson that this is a suitable case for chemotherapy.

As you know, Darier coined the term tuberculid. He said there was some toxin that got to the skin which was responsible for the various types of tuberculids. Later it was suggested that attenuated organisms got to the skin and caused the lesions. Jadassohn then hypothesized that both the lesion and the destruction of the bacillus were a consequence of the allergic state of the host. I think that is more or less the prevailing view concerning the genesis of these lesions today. It should be realized that there is practically no evidence to support such a theory. One of the strongest objections against this theory is a simple common-sense logical one. As we all know, tuberculids of all kinds are rare disorders, yet the immunologic status of a person with a tuberculid by and large is no different than that of a person with tuberculosis without a tuberculid. Consider, then, all the patients with pulmonary tuberculosis but without any evidence of cutaneous tuberculids. Surely in many of them tubercle bacilli get to the skin, yet they do not develop tuberculids despite the fact the allergen is there and the appropriate immunologic status exists. This, to me, is just not reconcilable with Jadassohn's views as to the pathogenesis of these lesions.

Another point I should like to comment on is the so-called Jadassohn (Lewandowsky) law. This law, in essence, asserts that when organisms are being slowly destroyed under the influence of antibodies, tubercles will result. I should like to point out that there is no evidence for this proposition and much evidence against it. For example, if one immunizes a rabbit against pneumococci and then takes the serum from an immune animal and injects it into a normal animal, thereby passively immunizing the normal, and if one takes living virulent pneumococci and injects them into the passively immunized animal, one will find that they are destroyed without any trace of tubercle formation, yet these organisms are being destroyed because of antibody activity. Many additional examples could be adduced. Rich, in his book on "The Pathogenesis of Tuberculosis," points out that tubercle formation is a reflection of the quality of the antigen introduced rather than signifying anything as to the immune state of the host.

Finally, I should like to point out that Stokes, as long ago as 1919, pointed out that, while of course it was true that tuberculids develop in people with tuberculosis, he thought it likely that the tuberculid was actually the expression of some secondary infection or invading organism. I believe this view has much merit to it and should be studied.

Systemic Blastomycosis. Presented by DR. THEODORE CORNBLEET, DR. DAVID COHEN, and DR. H. K. MITCHELL (by invitation).

History.—The patient, D. K., a 19-year-old Negro boy, presented himself to the admitting service of Cook County Hospital with the complaint of two rapidly growing lesions on his face of three weeks' duration. The lesions, one on the right cheek and the other on the left, were discrete, round, markedly elevated, dark red in color, and on a sessile base. They were of a soft consistency, with slight verrucous tendency, and oozed serum and pus on pressure.

Physical Examination.—On examination, two additional lesions were found on the right shoulder and back of the neck. The patient then said he had a dry cough for about the same length of time, but denied any exposure to tuberculosis. His temperature was normal, and the essential physical findings consisted of dullness and diminished breath sounds in the left lower lobe with occasional fine rales in the lower lobe.

The patient was treated for syphilis in 1951.

Laboratory Findings.—Urinalysis was negative. Hemoglobin 82%; white blood count 11,200; differential: polymorphonuclears 59%; lymphocytes 31%; monocytes 4%; eosinophiles 5%. Sedimentation rate 14 mm. in one hour; hematocrit 43%.

Kahn and Wassermann tests were negative. Nonprotein nitrogen 24 gm. per 100 cc.; total protein 8.1 gm., albumin 4.2 gm., globulin 3.9 gm., per 100 cc. Culture from a lesion showed nonhemolytic staphylococci.

Chest film showed pleural effusion in the left lower lobe with associated lobar pneumonia, and pleural thickening on the left side. The heart and trachea were displaced to the left. No osseous pathology was found in the skull, chest, or pelvis.

Mantoux 1:1000 negative; coccidioidin 1:100 negative; blastomycin 1:1000 positive in 48 hours, 8 by 8 mm. raised edematous area.

Skin biopsy is presented. Additional skin smears reveal Blastomyces sparsely. Chest fluid smears revealed numerous Blastomyces. Blood culture reports are not available.

Sporotrichosis. Presented by Dr. Irene Neuhauser, and (by invitation) Dr. Leonard A. Becker.

History.—Mrs. K. L., aged 38, a housewife, was first seen in the office of one of us (L. A. B.) on Nov. 24, 1953. History revealed that late in August, 1953, on a windy day she was scattering straw on the lawn. About one month later she noticed a small, painless, crusted lesion surrounded by a reddish zone on the inferior aspect of the left breast. When the crust was removed, a "punched-out" ulcer remained and a new crust would develop. When the lesion failed to heal promptly, she consulted her family physician, who had cultures done at a local hospital. He then instituted potassium iodide and antibiotic therapy by mouth. The initial lesion began to heal slowly, but a second lesion appeared on the superior aspect of the left breast about two weeks after the initial lesion was discovered. The second lesion began as a small red spot which gradually became larger, purplish-red in color, tender, and firm. Potassium iodide dosage had been gradually increased up to 20 drops t.i.d., and then gradually reduced. Since a "dark-colored growth" on Sabouraud's media from the above culture had been considered to be a contaminant, and the patient had developed a new lesion, she was referred for diagnosis and treatment.

Physical Examination.—On Nov. 24, 1953, the patient presented a small, irregularly-shaped, erythematous, slightly scaly, infiltrated area on the inferior aspect of the left breast; on the superior aspect of the left breast was a purplish-red, tender mass with a dime-sized fluctuant central area and an indurated peripheral zone; on the medial aspect of the left breast were several erythematous papules. There was no regional adenopathy. There were a few erythematous papulopustules on the face and upper chest and back. Punch biopsies of the two breast lesions were done, and treatment consisting of wet compresses with boric acid solution followed by 3% iodochlorhydroxyquin (Vioform) in a hydrophilic base was instituted.

By Dec. 5, 1953, a fluctuant lesion had developed on the medial aspect of the left breast.

Laboratory Findings.—Smears and cultures on aspirated material from the lesion on the medial aspect of the left breast showed growth on Sabouraud's medium which was morphologically a Sporotrichum. Material obtained on Dec. 22, 1953, also produced a pure culture of the same organism. Animal (mouse and rat) inoculations and further myocological studies were done, and the organism has been identified as Sporotrichum schenkii. The presenters gratefully acknowledge the assistance of Dr. Esther Meyer of the Bacteriology Department, University of Illinois College of Medicine, and Research and Educational Hospitals.

On Dec. 18, 1953 potassium iodide therapy was resumed, after which no new lesions appeared. At the present time the left breast lesions are subsiding satisfactorily, and the patient is being maintained on potassium iodide drops, 30 t.i.d.

Diagnostic skin test with the polysaccharide of S. schenkii was performed on Jan. 18, 1954.

Chest x-ray on Jan. 18, 1954, was reported as negative for parenchymal, osseous, hilar, or superior mediastinal involvement.

Biopsy specimens and cultures are presented.

DISCUSSION

DR. A. C. CURTIS, Ann Arbor, Mich.: I did not see the patient at Cook County Hospital, but I might report on a resurvey of our stilbamidine-treated patients with systemic blastomycosis. Of five such patients 60% have remained well; 40% relapsed (one four times), and 3, or 60%, have had fifth nerve damage. This means that stilbamidine, from a chemotherapeutic point of view, is not entirely adequate or harmless, so other compounds must be sought. Our present interest in the nitrostyrene group may result in such drugs.

I recently saw a patient in Toledo with systemic blastomycoses who had been treated with 3 gm. of stilbamidine. His pulmonary lesions did not clear, so a lung resection was done.

The patient with sporotrichosis was most interesting for several reasons. We often think of sporotrichosis as an infection characterized by a primary lesion and satellite lymphangitis. There are other types, however, one of which is the tuberculoid. Although this patient has been treated, I believe that the disease is of the tuberculoid rather than lymphangitis type. There is no question about the etiology, since the organisms were present in the section. We have treated only one case of sporotrichosis with stilbamidine, giving 100 mg. a day for 10 days.

Recently two patients with proved sporotrichosis were seen in our clinic; one was a child with a solitary granulomatous lesion on the glabella, and in the other one, sent to us by Dr. Parkhurst of Toledo, the condition looked clinically like actinomycosis but was proved to be sporotrichosis. In the latter patient x-rays of the mandible showed decalcification similar to that seen in actinomycosis of the cervicofacial type.

Sporotrichosis may disseminate and produce multiple, widespread, cutaneous lesions as well as bone involvement.

DR. HARRY FOERSTER, Milwaukee, Wis.: I agree with Dr. Curtis that this is an example of systemic or tuberculoid sporotrichosis. This form of the disease, in which the skin lesions develop as a result of hematogenous dissemination, is extremely rare in this country, though the most commonly reported type seen in continental Europe. Cases reported in the United States are invariably of the localized lymphangitic type in which there is a sporotrichotic chancre at a site of cutaneous inoculation, presumably after an injury, followed by the formation of nodules along a lymphangitic cord. The history of this patient having worked with straw suggests that respiratory tract inoculation may have resulted through inhalation and cutaneous lesions following hematogenous dissemination from an inner focus of infection.

DR. IRENE NEUHAUSER: The patient's explanation of the source of her infection can be accepted as more than a possibility, for the location is a natural one if she was wearing a low-necked dress on a windy day. In reference to the positive skin test, the test was performed with the polysaccharides of Sporotrichum schenckii. A great deal of experimental work has been done with the polysaccharides of the different fungi causing the deep mycoses, but the polysaccharides of S. schenkii are the only ones which have been sufficiently purified for routine purposes. This material has been tested in a number of cases of deep mycoses and has shown no cross positives.

DR. THEODORE CORNBLEET: Some internists feel all cases of blastomycosis are really systemic. I do not believe all dermatologists agree with that opinion. Taking note of the toxicity of stilbamidine, we are modifying an old remedy for these deep mycoses. We give thyroid together with the iodides, and it is surprising what large doses of both these patients can take comfortably. We are encouraged with our results thus far. I believe x-rays useful, too, for the skin lesions.

Erythema Caloricum and Melanosis Calorica. Presented by DR. S. W. BECKER.

History.—The patient, J. B., aged 19, had a giant cell xanthomatous tumor of tendon sheath origin removed from the dorsum of the left hand on Jan. 26, 1950. On Sept. 12, 1950, she developed cellulitis in the region of the scar. On Aug. 12, 1951, the tender scar was excised. In November, 1951 she developed lymphangitis and thrombophlebitis of the left forearm, which did not respond to antibiotics but did respond to heat and local measures.

On Dec. 21, 1951, she developed swelling of the right forearm with a mottled appearance, and a feeling of tightness in the axilla. She believes the mottled pattern appeared before heat was applied. Diagnosis was made of recurrent lymphangitis; the scar was excised again, and a biopsy of the cephalic vein was done. Pathologic diagnosis was "organizing thrombus in a minute vein." There was no histological evidence of tuberculosis or fungus disease.

In July, 1952, she sustained a blow on the forehead. A persistent ulcer yielded Gram-positive cocci and Gram-negative bacilli. It failed to heal under various treatments, but after excision, skin grafting, etc., it eventually healed in May, 1953.

She has had amenorrhea for two years. The present attack began one week before Thanksgiving, 1953, with tenderness and a red and brown network on the left forearm and fever. During her attacks her temperature rises to between 100 and 101 F. She has lost 30 lb. (13.6 kg.) of weight during this school year.

Physical Examination.—The patient presented an erythematous and brown vascular network on the left forearm and arm with a keloid on the left forearm at the site of biopsy of the vein.

Laboratory Findings.—Hemoglobin 12.8 gm. per 100 cc. (82%); red blood cell count 4,470,000; white blood cell count 10,150; differential: polymorphonuclears 63%; polymorphonuclears, nonsegmented 6%; eosinophiles 3%; lymphocytes 25%; mononuclears 3%.

Kahn test was negative on several occasions. The spinal fluid was normal. Various bacteriological, agglutination, and virus and Rickettsial tests were negative. Mantoux, 1:100,000 and 1:10,000, negative.

Roentgenogram of the left hand and arm was negative.

DISCUSSION

DR. S. W. BECKER: Dr. Webster just asked me whether this pigment will be permanent. In ordinary erythema caloricum, which used to be called erythema ab igne, the lesions are brown. One does not see the gray tint which you see in Riehl's melanosis. There the pigment will last for a long time. Here it clears up quickly. When I first saw the patient I thought she had erythema caloricum, but she said when she gets the attacks she develops these retiform plaques. That brings up the question of livedo racemosa, which subject I have discussed (Becker, S. W.: Generalized Telangiectasia: A Clinical Study with Special Consideration of Etiology and Pathology, ARCH. DERMAT. & SYPH. **14**:387, 1926). If it is livedo racemosa, it would probably not remain so localized and there would be some reaction in between the various attacks. With livedo racemosa there is obliterative change in the arteries between the dermis and the subdermis.

Urticaria Pigmentosa with Bone Lesions, Gastrointestinal Symptoms and Splenomegaly. Presented by DR. SAMUEL M. BLUEFARB, and (by invitation) DR. MELVIN R. SALK.

History.—The patient is a 30-year-old white man who was seen because of chronic fatigue, which has been worse in the past year, and chronic gastrointestinal difficulties, gasiness, bloating, eructation, flatulence, and constipation, all since the age of 11 or 12 but in the past five years with increasing severity. There also developed intermittent episodes of explosive diarrhea associated with cramps, nausea, and vomiting. Since 1948 he has had intermittent low-back pain (bilateral sacroiliac in location). He related that as far as he could recall his skin troubles became apparent at about the age of 11 or 12, the age at which he first remembers gastrointestinal difficulties, and that the quality of each disorder seemed to be parallel.

He was first properly diagnosed at the University of Iowa, and then more recently in February, 1952, thoroughly investigated by Dr. Sture Johnson of the University of Wisconsin. The patient had been referred to Dr. Johnson by the Orthopedic Department, where the patient had been seen for back pain. Complete investigation at Wisconsin, including peripheral blood and bone-marrow studies, porphyrin determinations, urinalyses, blood chemistries, x-rays, skin biopsy, etc., revealed only the following abnormal findings: urticaria pigmentosa with its attendant periodic acute urticaria and pruritus; an alkaline phosphatase of 8.2 B. U.; x-ray evidence of antral sinusitis; vertebral, clavicular, and rib osteosclerosis with a few minor changes in one femur; positive skin biopsy. Here, as with us later, efforts to obtain a bone

biopsy were to no avail. A variety of therapeutic regimes, including toluidine blue, PABA, cortisone (Cortone), a bromine derivative of diphenhydramine hydrochloride (Ambodryl), here and elsewhere, were without obvious beneficial effect.

Physical Examination.—The patient presented the diffuse skin picture of telangiectatic type urticaria pigmentosa, rather marked dermographism, marked bilateral nasal mucosal and turbinate congestion with obvious postnasal discharge, a short soft apical systolic murmur, a scaphoid moderately soft abdomen with a semifirm, somewhat tender spleen two to three fingers below the left costal margin on deep inspiration. Proctosigmoidoscopy to 10 inches revealed spasm, excessive mucus, increased mucosal friability, and diffuse mottling, some of which was prominent enough to almost suggest infiltrations, from 5 to 10 in. (12.5 to 25 cm.).

Laboratory Findings.—Urinalyses were normal; porphyrins negative. Hemoglobin 16.8 gm.; white blood cell count 9,900 to 12,900, with differentials showing some polymorphonuclear increase and slight eosinophilia. Red blood cell count 5,140,000 to 5,510,000. Hematocrit 53 to 54%.

Fasting blood sugar 93.4 mg., total cholesterol 149 mg., nonprotein nitrogen 49 mg., and later 32.4 mg., per 100 cc. Corrected sedimentation rate 6 to 11 mm. in one hour; stools: benzidine 2+ on general diet, unable to demonstrate Endamoeba histolytica or other parasites or pathogens. Nine smears stained by various techniques failed to reveal presence of mast cells.

X-rays: Skull negative; heart and lungs negative; generalized somewhat cystic osteoporosis of ribs, with some coarsening of trabeculae and stippling, more pronounced on the medial side of clavicles, and similar changes in thoracic and lumbar vertebrae.

DISCUSSION

Dr. Sture Johnson, Madison, Wis.: This patient was referred to me because of his skin condition by the Orthopedic Department, where he was seen because of low-back pain. A diagnosis of urticaria pigmentosa was made by me and proved by biopsy. The x-ray reports of the lower ribs, all lumbar vertebrae, pelvic bones, and upper ends of the femurs revealed finely mottled osteosclerosis compatible with osteoblastic metastases or myelofibrosis. These changes subsequently were shown to be characteristic of the changes reported by others in urticaria pigmentosa. Permission for bone biopsy was never obtained. This study should be done. Toluidine blue, paraaminobenzoic acid, cortisone, and Ambodryl did not alter the skin or bone changes.

Dr. A. J. Reiches, St. Louis, Mo.: The late Dr. Engman Sr. made the statement that all cases of urticaria pigmentosa did not urticate at all times when rubbed. The lesions of these patients with urticaria pigmentosa may urticate in the morning, for example, and that same afternoon the same lesions may not, in many cases, urticate. The following day the phenomenon of urticaria may again be produced.

In this patient I was unable to elicit the urtication phenomenon by rubbing these lesions.

Dr. Clark Finnerud: I believe Dr. Reiches has a point, that it is possible for a patient with urticaria pigmentosa to urticate at one time upon scratching the lesions and not at another time. Perhaps that and the following can be explained by Dr. Rostenberg. A member of my family was troubled with hives for several months and showed no response whatsoever to everything I knew about in the way of treatment. She was extensively tested against food and inhalant allergens by one of our leading allergists, and on one day gave a positive reaction to every agent. When these tests were repeated a few days later, every one showed a negative reaction. She remained free from eruption only after the correction of a focus of infection which was discovered in the ethmoids, an infection which had been asymptomatic.

Years ago I summarized the findings of the 308 cases found in the world literature (Arch. Dermat. & Syph. **8**:344, 1923), and noted none similar to this most unusual case presented today. Were it not for the numerous mast cells present in the sections, one might have good reason to suspect this case as being something other than urticaria pigmentosa.

Dr. Harold Shellow: You can see from the discussion that there are various ideas as to what this disorder might be. I think that it can be explained as a disorder other than urticaria pigmentosa. At a first glance, I was struck by its retiform appearance which brought to mind

parakeratosis variegata, but the flat-topped, scaling papules were lacking. Evidence of urtication in this patient's eruption is less marked than that seen in a typical urticaria pigmentosa, and I believe he has lost the characteristic changes of that disorder and has entered a sequelous stage of telangiectasia described as telangiectasia macularis eruptiva perstans. I have been interested in this disorder for some time, and, though some observers feel that telangiectasia macularis eruptiva perstans is merely a variant of urticaria pigmentosa, I feel that the distinct clinical, pathological changes, and the course of the former disorder should readily distinguish it from the latter. The diminution or the absence of mast cells and the marked telangiectasis present in telangiectasia macularis eruptiva perstans clearly separates it from urticaria pigmentosa. I believe that it should be considered as an entity. Some years ago, a case shown before this society by the late Dr. Oppenheim and later published in the *British Journal of Dermatology*, which I reviewed, followed the administration of tripelennamine (Pyribenzamine), but I do not think it fits into the Parks-Weber telangiectasia macularis eruptiva perstans. The case presented is unique in that bone, spleen, and gastrointestinal changes exist. Since some feel that heparin disturbance may be the underlying cause for the development of telangiectasia macularis eruptiva perstans, perhaps those internal organs are also the seat of pathological changes due to heparin changes.

Dr. Theodore Cornbleet: The mast cells so plentiful in the lesions of urticaria pigmentosa are said to contain heparin. However, we were unable to effect any appreciable change in our patients by treating them with toluidine blue, though others laid claim to doing so. Nor were we able to demonstrate any coagulation-retarding properties in the extracts from the lesions.

Dr. Adolph Rostenberg: One word on urtication. It has been recently shown that mast cells secrete not only heparin but also histamine. When the cell releases this histamine, urtication may develop, but if the supply of histamine becomes depleted, then further stimulation will not cause urtication until the supply becomes replenished, hence the variability of the urtication.

Dr. Samuel M. Bluefarb: The interesting fact is that urticaria pigmentosa is no longer primarily a skin disease; with the increasing number of reports relating to bone and gastrointestinal involvement it can be regarded as a systemic disease. This patient has involvement of the bone, gastrointestinal tract, splenomegaly, and, probable involvement of the reticuloendothelial system. The French writers in particular have noted involvement of the reticuloendothelial system and have reported patients having leukemia associated with urticaria pigmentosa.

Pityriasis Lichenoides et Varioliformis Acuta (Habermann). Presented by Dr. Julius E. Ginsberg.

History.—Mr. M. C., white man aged 40, has a generalized eruption of six weeks' duration. The lesions vary in appearance and are variably erythematous, telangiectatic, scaly, and crusting papules. They are most concentrated on the extremities. Itching is not pronounced. The lesions were noted in abundance initially one morning when the patient "woke up." The patient was receiving no internal medications or injections when the eruption appeared.

Laboratory Findings.—Routine laboratory tests are normal. No biopsy has been done yet.

DISCUSSION

Dr. Edward A. Oliver: Fred Wise, in a discussion of our paper read at a meeting of the American Dermatological Association in 1930, stated that he thought a better name for the disease was parapsoriasis varioliformis. Both Dr. Senear and I agree with this. This patient shown here today is a fairly good example of the disease. He shows evidence of hemorrhagic crusting and a maculopapular eruption on the abdomen and arms. The outstanding picture is a generalized eruption, the most characteristic of which is a papular lesion with a tendency to crusting, necrosis, and hemorrhage. This patient showed most of these lesions today, and I agree with the diagnosis.

Dr. Adolph Rostenberg: I agree with Dr. Oliver that there is a definite entity, namely, acute pityriasis lichenoides, which is related to and can convert into chronic pityriasis lichenoides. However, as Ingraham pointed out, it is probably unrelated to the rest of the parapsoriases. It has a different appearance and prognosis. Now, no matter what type of parapsoriasis you call it,

so long as the name parapsoriasis is in the label there is an implication that this condition is related to the other parapsoriases, which it probably is not. Hence, I agree with Ingraham, it would be better to call it pityriasis lichenoides either acute or chronic.

Hyperthyroidism with Nail Changes. Presented by DR. SAMUEL M. BLUEFARB, DR. A. L. GOLDBERG, and DR. H. K. MITCHELL (by invitation).

Raynaud's Phenomena. Presented by DR. DAVID OMENS, and (by invitation) by DR. HAROLD OMENS and DR. HAROLD MARKS.

Cutaneous Horns. Presented by DR. THEODORE CORNBLEET and (by invitation) by DR. SIDNEY BARSKY and DR. HAROLD MARKS.

Xanthomatous Biliary Cirrhotic Pruritus. Presented by DR. HERBERT RATINER and (by invitation) by DR. HAROLD RODIN and DR. LEONARD HOIT.

Chronic Leg Ulcer and Sickle Cell Anemia. Presented by DR. SAMUEL M. BLUEFARB and (by invitation) DR. A. L. GOLDBERG and DR. LEONARD HOIT.

A Case for Diagnosis (Micropapular Tuberculid?). Presented by DR. GEORGE C. WELLS (by invitation) and by DR. STEPHEN ROTHMAN.

Morphea with Beginning Disseminated Generalized Scleroderma? Presented by DR. EDWARD A. OLIVER.

Unilateral Scleroderma in Patches. Presented by DR. THEODORE CORNBLEET.

Lichen Sclerosus et Atrophicus. Presented by DR. H. J. BURSTEIN.

Pseudoscleroderma? Presented by DR. THEODORE CORNBLEET and (by invitation) by DR. SIDNEY BARSKY and DR. LEONARD HOIT.

Facial Granuloma with Eosinophilia. Presented by DR. SAMUEL M. BLUEFARB.

A Case for Diagnosis (Facial Scars). Presented by DR. MARCUS R. CARO.

Sarcoidosis. Presented by DR. H. J. BURSTEIN.

Idiopathic Multiple Hemorrhagic Sarcoma of Kaposi. Presented by DR. HERBERT RATINER.

MANHATTAN DERMATOLOGICAL SOCIETY

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Jan. 12, 1954

Myelogenous Leukemia. Presented by DR. ORLANDO CANIZARES and DR. MAURICE J. COSTELLO.

A. R. P., a girl aged 14, was operated upon in February, 1953, for acute appendicitis. Her postoperative course was uneventful for eight days, at which point she developed an erythematous eruption on the forehead, left arm, and left side of the chin, associated with fever and chills. The diagnosis of penicillin reaction was considered, but because the lesions were like erythema nodosum and the patient had joint pains, the diagnosis of rheumatic fever was made. Treatment with salicylates and corticotropin (ACTH) was instituted, and the symptoms improved. There were three recurrences, each with extensive cellulitis-like lesions, some covered with large bullae, and each time treatment with corticotropin and cortisone led to complete remission. The laboratory tests were normal except for severe anemia and on one occasion an increase of the white blood cell count. A biopsy was performed and the diagnosis of possible chronic relapsing febrile panniculitis was made.

After a short period of hospitalization at St. Vincent's Hospital, where the L.E. cell was reported present in the blood on two occasions, the patient was transferred to Lenox Hill Hospital, where these findings were not confirmed. The patient recovered from another attack with large doses of corticotropin and cortisone, and repeated blood transfusions. The sternal marrow was reported extremely hyperplastic, with a pronounced increase in the granular cells, particularly of the immature type, and a differential white cell count of the peripheral blood showed 75% polymorphonuclear leucocytes, 12% myeloblasts, 9% lymphocytes, and 3% monocytes. The hematologist, Dr. Carl Reich, felt that from this examination and successive ones which showed an increase of myeloblasts, the diagnosis of myelogenous leukemia should be considered. Successive white cell counts were 20,000, 30,000, and 60,000. The patient received 75 mg. daily of 6-mercaptopurine (Purinethol), with a great decrease in the white cell count. Two large lesions disappeared rapidly after x-ray treatment. Roentgenograms of the spine showed leukemic infiltration.

At present the patient presents residual areas of pigmentation and purpuric macules on the areas previously affected. There is one granulomatous lesion on the left foot.

DISCUSSION

DR. PAUL GROSS: Cutaneous manifestations are comparatively rare in myelogenous leukemia. The tumor-like appearance of the lesions the patient presents tonight is that found in myelogenous leukemia, in addition to hemorrhagic eruptions.

DR. JACK WOLF: This is a rare picture. The diagnosis can be reached only by careful study such as Dr. Canizares has made. We are all fortunate to have seen it.

DR. DAVID BLOOM: I would suggest the administration of triethylene melamine. If it is carefully given there is much less danger of by-effects than with any other nitrogen mustard.

DR. SAMUEL M. PECK: You have to watch the melamines because they can cause thrombocytic leucopenia. In some instances we have found them quite toxic.

DR. A. C. CIPOLLARO: The textbooks mention the association of cutaneous lesions with myelogenous leukemia, but this is the first time I have seen it. In the lymphoblastomas in general, the lesions change in character, at one time being those of erythema multiforme, another time erythema nodosum, and at still another the definite infiltrated plaques that you see in mycosis fungoides. This has been a most instructive case, and I am very thankful to Dr. Canizares for having presented it.

DR. PERRY SACHS: I am unable to correlate, in this case, the unusual features of scarring and atrophy which are present under the left arm. As suggested, previous microscopic studies showed a leukemid or nonspecific reaction. However, I am confident the granulomatous lesion on the leg would show an infiltration of leukemic cells.

DR. ORLANDO CANIZARES: We have been following this case since last year. The original complaint was an attack of what was called appendicitis, which was really one of the symptoms of the disease. It is unfortunate that there was no histologic examination. Shortly afterward the patient developed lesions on the skin, and every one, as Dr. Cipollaro mentioned, has been different. It is interesting that she has had these nonspecific lesions all along when the blood count was not typical. As soon as the changes of leukemia appeared in the blood picture, the lesions started to look like those of leukemia cutis. They melted away with roentgen therapy. I have the impression that the early administration of cortisone, although it benefited the patient, also suppressed the hematologic signs of the disease. The early diagnosis of leukemia was made by sternal puncture.

DR. DAVID BLOOM: Was that done before or after the peripheral blood showed changes?

DR. ORLANDO CANIZARES: The diagnosis of leukemia was suspected, and the sternal marrow examination was performed. She had had a previous elevation of the white cell count which was nonspecific and thought to be a reaction to cortisone.

Generalized Neurodermatitis with Lichen Amyloidosis of the Extremities. Presented by DR. SAMUEL M. PECK.

R. L., a woman aged 28, has had "skin trouble" for 25 years. The patient has hard, scaly, red patches over the flexor surfaces of the elbows, front of the chest, and face, associated with swelling of the ear canals and eyes when the itching becomes severe. There is generalized eczematization of the skin. In addition, there is definite amyloidosis on the legs. In the past few months there has been an associated furunculosis. Numerous enlarged glands are felt in the postcervical region. The patient states these have always been present, but without fever. There are no allergies and no food sensitivities that she knows about, and she is otherwise well. A general physical examination was normal.

The blood count, urinalysis, and stool examination were normal. Roentgenograms of the chest and soft tissues of the neck showed no abnormality. The globulin was 3.4 gm. per 100 cc., with a normal A/G ratio. Thymol turbidity was normal, as was mucoprotein and protein-bound polysaccharide. The zinc sulfate turbidity was slightly increased, in conformity with the slight elevation of gamma globulin. The basal metabolic rate was +3%, nonprotein nitrogen 24, cholesterol 188 mg. per 100 cc., and the Wassermann reaction of the blood was negative.

Biopsy showed a moderate hyperkeratosis. The epidermis was regularly acanthotic, with thinning of the rete pegs and some fusion. In some interpapillary areas there were aggregates of homogeneous collagen suggestive of amyloid. Diagnosis: Amyloidosis cutis (papillary form).

DISCUSSION

DR. SAMUEL M. PECK: We first suspected flat warts.

DR. JACK WOLF: I am glad to hear the diagnosis first entertained was flat warts, because that was the one I entertained tonight. The histologic diagnosis of amyloidosis must be accepted.

DR. ADRIAN BRODY: The lesions on the forearm resemble those of papular neurodermatitis.

DR. JOHN W. DOUGHERTY: I would suggest occlusive dressings, in line with the work reported at the New York Academy of Medicine; the attempt was made to treat by infiltrating with cortisone and bandaging. With just the occlusion alone the patients got well. Perhaps the scratch mechanism plays a role.

DR. DAVID BLOOM: Such verrucous papules are not infrequently seen in neurodermatitis.

DR. PERRY SACHS: It is difficult to understand how any type of treatment could cure amyloidosis, which causes permanent change. Perhaps treatment eradicates the secondary lichenification, with apparent improvement, and, in a small lesion, suggestive cure.

DR. ORLANDO CANIZARES: There may be papular lesions in neurodermatitis, and it may be a type of change secondary to neurodermatitis. As far as treatment is concerned, perhaps some lesions could be treated with solid carbon dioxide.

DR. PAUL GROSS: This case is unusual because of the appearance of discrete papules of lichen amyloidosis appearing in the course of disseminated neurodermatitis. The more common differential diagnosis encountered is that between lichen simplex chronicus and its rare variety of lichen moniliformis on the one hand, and lichen amyloidosis on the other. Awareness of the possibility of localized amyloidosis has greatly reduced the diagnosis of so-called lichen moniliformis. I would recommend the treatment with podophyllin ointment as suggested by Dr. Garbe.

Case for Diagnosis (Lymphocytic Infiltration of the Skin? Lupus Erythematosus?). Presented by DR. PAUL GROSS.

Neurofibromatosis. Presented by DR. DAVID BLOOM.

Case for Diagnosis (Lupus Erythematosus?). Presented by DR. JACK WOLF.

MINNESOTA DERMATOLOGICAL SOCIETY

Merriam G. Fredricks, M.D., President

Harold G. Ravits, M.D., Secretary

Duluth Meeting, Sept. 12, 1953

Acute Lupus Erythematosus with Neurologic Complications. Presented by DR. JOHN F. SCHMID, Duluth.

Mrs. E. G., a 26-year-old housewife, native of Michigan, in September, 1951, noted cyclic changes in the circulation of the digits upon exposure to cold—blueness, then pallor, followed by rubor on exposure to heat. In December, 1952, generalized stiffness, aching and swelling of joints appeared. About March 1, 1953, a low-grade fever and fatigue were noted. Periorbital edema, erythema of the face, and impaired hearing developed about 10 days prior to hospitalization. Diarrhea and petechiae on the fingertips were noted shortly before hospitalization on March 13, 1953.

The past medical history revealed that she used five to six Anacin tablets (a mixture of acetophenetidin, acetylsalicylic acid, caffeine, and quinine sulfate) per day during the illness, that her normal weight was 120 lb. (54.4 kg.), that she had two normal pregnancies, and a background of insecurity as an only child of an elderly righteous family.

Examination at the time of hospitalization disclosed a toxic, anxious young woman with a temperature of 102 F. Petechiae, exfoliation, and cyanosis were present on all digits. Circumorbital edema with bluish-red color extended over the cheek and nose. The edematous conjunctiva protruded from the lids. Retinal edema without a choked disc and white exudates were present on the right. Pitting edema of the ankles was present. Neurological examination disclosed an eighth nerve palsy, severe generalized hyporeflexia, and weakness. Clinical diagnosis of acute sinusitis, and observation for a collagen disease, rheumatic fever, trichinosis, and polyarteritis were entertained.

Laboratory examinations disclosed a leucocyte count of 5,350, sedimentation rate of 90 per hr., negative blood culture and agglutinations for brucellosis and for a reversal of the A/G ratio. Spinal fluid showed a protein of 73 mg. per 100 cc., a negative VDRL test and gold curve of 5543200000. The ECG showed toxic changes. Sinus x-ray films showed haziness of the right antrum and ethmoid cells. L. E. tests from iliac marrow and buffy coat preparations were negative.

The patient's condition deteriorated during the first 72 hours of hospitalization. The leucocyte count was 2,800, joint pains and fever remained prominent, and she appeared moribund.

Therapy with 40 mg. of intravenous corticotropin (ACTH) and 200 mg. of cortisone was begun on the fourth hospital day. Forty-eight hours later the white count was 8,800, the fever low, joint swelling subsiding, but facial erythema and edema unchanged. Mental confusion and euphoria appeared and became progressively worse, leading to reduction of the cortisone dosage to 100 mg. per day. Improvement in the erythema of the face continued until about April 5, when it recurred, and this with its accompanying leucopenia was corrected by increased cortisone dosage. Twice weekly corticotropin gel dosage was used to stimulate the adrenals. It was found that dosage of cortisone below 100 mg. per day allowed the eruption, fever, and leucopenia to recur. Psychiatric improvement occurred when she was reunited with her parents and children. Increasing activity was begun in July, but muscular weakness and fatigability have persisted. The hearing and vision recovered.

Muscle biopsy did not show findings consistent with dermatomyositis. The L. E. phenomenon was demonstrated on Sept. 9, 1953.

Acrosclerosis: Failure of Cortisone to Modify. Presented by Dr. John F. Schmid, Duluth.

L. A., a 17-year-old, white girl, high school student, developed Raynaud-like circulatory changes in the hands following swimming in July, 1949. By March, 1950, a relatively fixed pallor of the fingertips to middle phalangeal joint was noted, accompanied by tingling and numbness. Ulceration and fissuring of the third digit of each hand was seen in September, 1950. Subsequently the toes began to exhibit cyclic color changes, incited by exposure to cold.

Bilateral dorsal sympathectomy (T 2 and 3) was undertaken in March, 1951. Tonsillar hypertrophy and cervical adenopathy were noted. Blood pressure was 128/78 mm. Hg. Relief of pain and healing of the fingertip ulcerations followed. A stiffening of the skin of the hands was noted at this time. Vasodilators such as Roniacol tartrate (the tartaric acid salt of the alcohol corresponding to nicotinic acid) and benzazoline (Priscoline) were administered with negligible effect.

In September, 1952, she became conscious of a widespread stiffening of the skin involving the face, neck, upper chest, hands, forearms, and lower legs. Examination in January, 1953, disclosed a picture of diffuse scleroderma plus acral cyanosis or pallor, depending on the outdoor temperature, also stiffness of the fingers and toes with multiple ulcerations of fingertips. The weight was 131 lb. (59.4 kg.), the blood pressure 98/60 mm. Hg. No dysphagia was noted.

Therapy with cortisone was initiated at 200 mg. per day in February, 1953, and continued for one month. The course was repeated in April and May at 100 mg. per day level.

Laboratory examinations, including cryoagglutinations, were negative. The blood calcium was 9.6 mg. per 100 cc., alkaline phosphatase 3.7 K.A. units, sodium 139, and potassium 4.4. mEq. per liter.

She has recently been studied at Gillette Hospital, and lumbar sympathectomy has been proposed.

Lupus Erythematosus. Presented by Dr. Frederic T. Becker, Dr. Merriam G. Fredricks, and Dr. Joseph G. Brennan, Duluth.

Mrs. J. J., a woman aged 49. Onset in 1935, during first pregnancy of erythematous lesions on tips of fingers and toes which extended to involve face, legs, and arms. Patient had a spontaneous abortion and her condition improved; she, however, had an exacerbation during her second pregnancy a year later. Since then she had periodic and persistent attacks with exacerbation during her menses.

She was treated with gold with a considerable reaction. Was worse on PABA, with marked dissemination of lesions to involve face, legs, arms, buccal mucosa. Unimproved on cortisone (Cortone) ointment, pantothenyl alcohol (Panthenol), testosterone, vitamin E, and quinacrine (Atabrine [50 to 100 mg. q.i.d.]). During the latter therapy, she developed arthritis and exacerbation of her skin condition. Histologic sections were shown.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I have seen two patients with acute systemic lupus erythematosus who have developed the neurologic complication, Guillain-Barré syndrome. This is characterized by alterations of the protein and cell count in the spinal fluid, and clinically the patients show neuronitis, with symptoms of exquisite causalgia in the extremities. This syndrome is not specific for lupus but may be associated with a variety of nonrelated disorders. Patients with acrosclerosis are not benefited by sympathectomy. Such treatment relieves the Raynaud phase of the disease but does not affect the progression of the scleroderma.

DR. JOHN F. SCHMID, Duluth: Our consulting neurologist did agree that she had findings of the Guillain-Barré syndrome in the spinal fluid and in the neurological changes. We thought there might be focal vascular lesions in the central nervous system when we had a look at the retina.

Commenting on the patient with acrosclerosis, I would be interested in hearing some opinions as to the usefulness of sympathectomy in treatment of these patients. Does it have a totally temporary value?

DR. H. E. MICHELSON, Minneapolis: In reading the history of Dr. Schmid's patient, I could not help thinking of a warning that I believe should be sounded. If a patient comes to my office, upon whom a diagnosis of systemic lupus erythematosus is suspected, and especially if the patient is very sick, I would like to suggest that one do the most direct test first and if that is positive (for example the L. E. test) there is no need of going further. I think it is dangerous to do muscle biopsies and spinal punctures and so on in attempting to diagnose the very sick patient.

DR. STURE A. M. JOHNSON, Madison, Wis.: I think neurological findings are either being seen or recognized more frequently in patients with lupus erythematosus. Our department of neurology is even now wondering whether or not multiple sclerosis is lupus erythematosus of the spinal cord. Recently we had a patient with lupus erythematosus who complained of numbness, tingling, weakness, and difficulty in urination. The spinal fluid showed a total protein of 175 mg. per 100 cc., sugar 39 mg. per 100 cc., 16 white cells, and colloidal gold test showed 5555432100. At postmortem the meningeal vessels showed thickening, perivascular infiltration, and fibrinoid changes within the walls. Vessels contained thrombi. The posterior funiculi showed myelomalacia, and there was a loss of ganglion cells in the posterior horns. More spinal fluid examinations might reveal fairly frequent involvement of this tissue in lupus erythematosus. The fact that psychosis may develop in patients with L.E. is now well known and these may develop independent of corticotropin or cortisone therapy.

The patient with acrosclerosis also has scleroderma. The child's lips, nose, and face showed changes characteristic of hidebound disease. The problem is whether we have a patient who first developed acrosclerosis and then scleroderma or sclerodactylia and then scleroderma. In any event, scleroderma is becoming more evident, according to the clinical course and the parent.

In the other patient, we see Raynaud-like symptoms of a peripheral vascular disease occurring in a patient with L.E. I have come to feel that these changes are seen frequently in these patients during changes in weather. In one instance, amputation of a foot even became necessary. The dystrophic changes in this patient's fingers suggest dystrophic epidermolysis bullosa.

DR. JOHN F. MADDEN, St. Paul: I think that the Raynaud-like syndrome associated with L.E. in any form is very rare.

DR. JOHN KRAFCHUK, Minneapolis: I would like to ask Dr. Johnson what the spinal fluid findings are in neurological involvement.

DR. STURE A. M. JOHNSON, Madison, Wis.: The patient I am describing had a first and mid zone colloidal gold curve with a total protein that was above 50 and an increase in cells.

DR. JOHN KRAFCHUK, Minneapolis: On the subject of neurologic involvement in L.E., we have done electroencephalographic studies on 13 cases with systemic involvement in which the nervous manifestations in terms of irritability and psychic manifestations were rather marked, and the electroencephalograms were all completely normal. One case was cited in which an electroencephalogram was done at a time of relatively mild activity. The patient developed toxic psychosis with cortisone; she became completely uncontrollable and had to be committed to the psychiatric ward. The electroencephalogram was repeated at the height of this toxicity and still remained perfectly normal; so the EEG does not help in this particular problem.

Pemphigus Foliaceous. Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Pemphigus Vulgaris. Presented by DR. MERRIAM G. FREDRICKS, DR. FREDERIC T. BECKER, and DR. BRENNAN, Duluth.

Dermatitis Herpetiformis. Presented by DR. MERRIAM G. FREDRICKS, DR. FREDERIC T. BECKER, and DR. BRENNAN, Duluth.

Case for Diagnosis: Prurigo Ferox? Presented by DR. G. C. DOYLE, Duluth.

Acrodermatitis Chronica Atrophicans, Contact Dermatitis Petroleum Products, Failure to Respond to Penicillin. Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Pustular Psoriasis. Presented by DR. MERRIAM G. FREDRICKS, DR. FREDERIC T. BECKER, and DR. BRENNAN, Duluth.

Nevoxanthoendothelioma. Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Secondary Xanthomatosis? Early Biliary Cirrhosis. Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Tuberous Xanthomatosis with Hypothyroidism? Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Lymphoblastoma. Reticulum Cell Sarcoma? Mycosis Fungoides? Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Erythroplasia of Queyrat? In a Female. Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Eosinophilic Granuloma: Solitary Type. Presented by DR. FREDERIC T. BECKER, DR. MERRIAM G. FREDRICKS, and DR. BRENNAN, Duluth.

Sarcoma. Presented by DR. MERRIAM G. FREDRICKS, DR. FREDERIC T. BECKER, and DR. BRENNAN, Duluth.

Melanoma. Presented by DR. MERRIAM G. FREDRICKS, DR. FREDERIC T. BECKER, and DR. BRENNAN, Duluth.

Merriam G. Fredricks, M.D., *President*

Harold G. Ravits, M.D., *Secretary*

Nov. 20, 1953

Chronic Discoid Lupus Erythematosus in a 16-Year-Old Girl. Presented by UNIVERSITY HOSPITAL STAFF.

E. C., a 16-year-old white native-born girl, was first noted to have a red scaly lesion under the right eye in May, 1941, at the age of 3 years. There were no associated systemic manifestations. Six months previously she had scarlet fever, and just prior to that chickenpox and pertussis.

From 1941 to 1944, when she was first seen at the University Hospitals, new lesions appeared on the face, scalp, behind the right ear, on the chest and back, some of them healing spontaneously and leaving atrophic scars. Diagnosis of lupus erythematosus was confirmed by biopsy. She was free of systemic complaints; temperature ranged up to 99.8 F. daily. A course of fever therapy with typhoid vaccine was given, with little effect. One white cell count of five showed a leucopenia (3,150). All other laboratory findings were normal (urine negative, albumin 4.6, globulin 2.5 gm. per 100 cc.). ESR ranged from 60 to 89 mm. per hour.

She was not seen again at the University Hospitals until 1953. During this time the original lesions persisted, with occasional development of new areas on the face. There have been no systemic complaints. In 1951 she underwent an appendectomy, with uneventful recovery.

Present laboratory data reveals the following: urine normal; hgb. 12.9; WBC 4,250, with a normal differential; ESR 38 mm. per hour; serum albumin 3.5, globulin 3.8 gm. per 100 cc.; STS negative; x-ray of chest negative.

Therapy with chloroquine in a dosage of 250 mg. per day was begun on Oct. 15, 1953. Some resolution has occurred.

Case for Diagnosis: Lupus Erythematosus. Presented by DR. C. D. FREEMAN, JR., St. Paul.

Mrs. McG., aged 35, mother of six children. This patient was first seen at the Dermatology service at Wilder Dispensary on Feb. 5, 1952, with a bald spot in the frontal area of one month's duration. A diagnosis of alopecia areata was made, and she was treated with ethyl chloride spray. On April 22, 1952, she was found to have an erythematous, annular lesion about the size of a quarter in the left axilla. In spite of various local applications, this lesion continued to grow until it reached a diameter of about 5 in. (12.7 cm.). On July 1, 1952, a new lesion about the size of the original lesion was noted adjacent to it.

Urinalysis at this time was essentially normal except for four or five pus cells. A hemogram showed 16.15 gm. hemoglobin, or 97%, RBC 4,740,000, WBC 5,760, PMN 58%, lymphocytes 38%, eosinophiles 3%, and basophiles 1%. On July 22, 1952, the patient was noted to have an erythema of the butterfly area of the face following a rather marked exposure to sunlight. On July 29, 1952, this had become worse and there were now lesions on the neck. A CBC done at this time was essentially the same as the previous one; sedimentation rate was 20 mm. per hour, sternal biopsy showed moderate myeloid and erythroid hyperplasia, no L. E. cells present. On August 5, 1952, total serum protein was 6.17 gm. per 100 cc., with an A/G ratio of 1:2. The patient was hospitalized on Aug. 8, 1952, when the eruption had spread to her arms and thorax. At this time the patient also stated that she had noted weakness since the onset of her eruption. She was placed on corticotropin (ACTH), which produced a slow but constant clearing of the lesions, and she was discharged from the hospital on Sept. 5, 1952. An L. E. cell test with peripheral blood was done during this period and was reported negative. Repeated urinalyses were negative except for occasional pus cells. The WBC done on Aug. 9, 1952, was reported to be 3,950, on Aug. 17, 4,500, and later ones varied between 6,700 and 9,950. Repeated A/G ratio's varied between 1:2 and 1:5; serum proteins were always in excess of 6.0 gm. per 100 cc.; sedimentation rate on Aug. 28, 1952, was reported as 31 mm. per hour.

On Sept. 2, 1952, a BMR was reported as —5 and blood cholesterol 138 mg. per 100 cc.; EKG done on Aug. 15, 1952, was reported as showing myocardial changes. This was repeated on Aug. 29, 1952, when it was reported low voltage but otherwise normal. The patient was discharged from the hospital on Sept. 5, 1952, when her skin was clear. When she was seen at the outpatient department, erythematous lesions of the eyelids were noted; the patient complained of weakness and some precordial distress. She was referred to the Medical Service for evaluation, and they more or less took over her treatment. She was treated with cortisone by mouth and by injection, as well as with corticotropin, without much improvement of her skin or physical condition. She was hospitalized in October, 1952, and again in February, 1953. X-rays of the chest and G.I. tract have been normal. Temperatures have run between 97 and 100 F. under various hospitalizations and when checked in the outpatient department. Blood serology tests have been consistently negative. A/G ratios remain in the neighborhood of 1:2. Sedimentation rates vary between 12 and 31 mm. per hour. Tests for porphyrins have been negative; agglutination tests for brucellosis have been negative; cephalin flocculation negative at 24 hours, and two at 48 hours. BUN 12 mg. per 100 cc.

Systemic Lupus Erythematosus. Presented by ANCKER HOSPITAL STAFF.

Mrs. J. O'N., aged 37, was treated in 1940 for a macular eczematoid rash of the face and neck with lid edema. This cleared and, except for chronic fatigue, the patient felt well until April, 1952, when she developed weakness of the left ankle, arthralgia of the hands, and dry erythematous eruption of arms and cheeks. By September, 1952, tiredness became a prominent symptom along with painful swollen joints of hands. Vague chest and abdominal pains also appeared. In June, 1953, bullous eruptions appeared on the arms, and the patient was put on cortisone therapy and rest, with marked improvement and disappearance of bullae.

Laboratory Findings: April, 1952 and on numerous subsequent examinations, L.E. cells: —; Haserick test: +. Urinary findings: albumin 2 +; casts: hyaline +, granular +; leucocytes +, erythrocytes 2 +. Sedimentation rate 70-110 mm. per hour; WBC 8,000-10,000; Blood albumin 4.2, globulin 3.3 gm. per 100 cc.; blood Wassermann: anticomplementary; VDRL: positive, undiluted only. Uric acid: 7.2-8.0 mg. per 100 cc. (father has gout). X-rays of chest: negative. EKG: negative.

Chronic Discoid Lupus Erythematosus Successfully Treated with Chloroquine Diphosphate. Presented by DR. JOHN F. MADDEN, St. Paul.

Miss H. A., aged 54, presented an eruption on the face and scalp which appeared in 1943 and progressed until September, 1953. General examination at the Mayo Clinic showed no other abnormalities. From 1943 to 1949 she received numerous injections of gold sodium thiosulfate. In 1950 she had 50,000 units of vitamin D daily over a long period of time. In 1951 she received 15 intramuscular injections of bismuth salicylate in oil; from August until November, 1952, she received 2 gm. of pantothenyl alcohol (Panthenol) t.i.d. The lupus erythematosus continued to progress during this time. In November, 1952, she was given 300 mg. of quinacrine (Atabrine) daily, and she continued to improve until she was lost track of in January, 1953. She was seen again in June, 1953, with a dermatitis on her forearms and hands which may or may not have been caused by quinacrine, which she had taken intermittently. She was next seen in September, 1953, and was given 25 mg. of chloroquine diphosphate b.i.d. The lupus erythematosus has practically healed as of this day, Nov. 20, 1953.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester: My experience indicates that quinacrine and chloroquine are the best treatment for chronic lupus erythematosus. About one-third of the patients are cleared, another one-third improved, and the rest resistant. Untoward reactions to either one are minimal. A patient may respond to chloroquine and not to quinacrine, or vice versa. In those who show systemic involvement, that is, fever, arthralgia, increased sedimentation rate, and positive L.E. phenomenon, I prefer not to use quinacrine or chloroquine.

The management of patients with systemic lupus erythematosus is a highly individual matter. If there is fever, arthralgia, fatigue, or visceral symptoms such as effusions, bed rest is mandatory and cortisone is the treatment of choice. On the other hand, if there is appreciable renal impairment, cortisone or corticotropin should be used with caution. It is quite evident that the demonstration of the L.E. phenomenon is not in itself an indication for steroid therapy.

DR. JOHN R. HASERICK, Cleveland: I agree with the diagnoses, but feel differently about the 37-year-old patient. I think that this woman is in a very precarious situation. There is already evidence of renal damage, and I believe in a matter of a few months she will succumb to the renal shutdown.

I believe that the 16-year-old girl should receive cortisone therapy continuously. The dosage should be regulated to just the amount necessary to control the manifestations of the disease. In addition to the cortisone, 10 units of corticotropin twice weekly may help to prevent acute flare ups.

DR. PAUL A. O'LEARY, Rochester: I believe that the 35-year-old woman has dermatomyositis, not lupus erythematosus. The weakness of the muscles of the arms, shoulder girdle, and back is pronounced, and morphologically she presents none of the characteristics of lupus erythematosus. The laboratory data, which are essentially normal, also favor the diagnosis of dermatomyositis.

Neither do I believe that cortisone will help this patient. Cortisone and corticotropin do not cure patients with cutaneous diseases, although occasionally they will produce and maintain a patient in remission. It must not be forgotten that both of these agents may produce serious complications, even death, irrespective of whether the dose is large or small, or given for a short time or long time. Lupus erythematosus is a protean disease with many phases which we endeavor to classify, depending on the clinical picture and the laboratory data, and so we say one type of case is acute, while the condition of another patient who appears less ill is subacute, and a third may be of the chronic disseminating type. Such a classification is loose, often not indicative of the actual situation, and may be misleading because of the frequency with which an acute case may become subacute or chronic, and vice versa. Accordingly, I question the justification of evaluating in percentages the results of treatment in a group of patients with a disease characterized by pronounced transient features in which clinical reversals occur spontaneously. When such patients are treated with drugs that are as unpredictable as cortisone and corticotropin, the objection seems greater. The subacute case may go into remission whether it is given cortisone and corticotropin, or whether the patient merely spends three months in bed.

DR. JAMES R. WEBSTER, Chicago: I would like to comment on the age of the 16-year-old patient. At the time of onset of her illness she was 3 years old. I know of one systemic case which began at the age of 10, and one discoid case which began at the age of 6. I have never heard of or seen discoid lupus erythematosus beginning at the age of 3. I would be interested to know if anyone has. At the meeting in Chicago Dr. Forman, who is president of the Dermatology Society in London, was asked about quinacrine. I think it is essentially the same as here. Introduction of quinacrine, as you know, for the treatment of L.E. was a definite mistake and accident in the first case.

DR. H. E. MICHELSON, Minneapolis: Lupus erythematosus is not a subject that lends itself well to extemporaneous discussion, because one must decide whether the person one is debating with is on the same ground. Dr. Haserick speaks in definite percentages, and it is almost impossible to be arithmetically correct in estimating results of therapy in this disease.

The 35-year-old patient brings up the question of biopsy specimens taken from areas which are not ordinarily involved by chronic lupus erythematosus. We have found that even when a lesion exists on the trunk the biopsy is more difficult to evaluate than when the specimen is taken from a lesion on the face.

In discussing dosage, I would not like to see the profession get the impression that cortisone for a patient with systemic lupus erythematosus is to be likened to insulin for diabetes. The drug as used in lupus erythematosus after a severe attack has found these patients to be desperately sick without certain dosage. The amount used does not restore them to complete health and keep them there.

DR. HAMILTON MONTGOMERY, Rochester: I understand that this woman has had an erythema on her back for some time. A histologic diagnosis of lupus erythematosus cannot be made on a transitory lesion or on a lesion that has only been present a few weeks. It is preferable to perform a biopsy on a lesion of a month's or more duration.

Lichen Sclerosis et Atrophicus. Presented by DR. HAROLD G. RAVITS, St. Paul.

M. S., 6 years old, was found to have skin changes about the vulva and anus approximately five months ago. The child's mother noticed occasional hemorrhagic changes in the affected areas. Vitamin A ointment is being used to keep the skin soft.

Linear Scleroderma. Presented by DR. JOHN F. MADDEN, St. Paul.

H. B., aged 7 years, presents a lesion of linear scleroderma appearing over the course of the sensory nerves, extending from the dorsal spine anteriorly to the midline on the left side. The eruption is of five months' duration, and there are no subjective symptoms.

Localized Scleroderma with Ulcerations and Bullous Formations. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. R. A., presents widespread localized scleroderma over the abdomen and chest of about six months' duration. Biopsies were done by Dr. H. C. Leiter of Sioux City, Iowa, which substantiated the diagnosis. The bullous lesions and ulcers were on the abdomen and chest only. BMR: 27%.

Morphea. Presented by DR. JOHN F. MADDEN, St. Paul.

Mrs. E. G., aged 55, presents an egg-sized patch of morphea on the left side of the abdominal wall just below the ribs and an irregular lesion covering most of the left breast at the point of its junction with the chest wall. The eruption is of 18 months' duration and there has been little change during that time. General examination was negative.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester: A practical classification of the cutaneous scleroses is as follows: (1) morphea, or localized scleroderma; (2) linear scleroderma; (3) hemiatrophies; (4) generalized, or systemic, scleroderma; (5) acrosclerosis. The patient with morphea of the pigmented nonsclerosed type causes diagnostic confusion because the patches of scleroderma are conspicuous by their absence. The patients with morphea characterized by cutaneous scleroses

as well as pigmentation have two features worthy of mention, namely, an occasional case will present bullae in the skin surrounding the plaques, and, second, complete involution of the hardened skin may occur without leaving clinically recognizable scars or pigmentation. My experience with quinacrine in the treatment of morphea is of too short duration for me to express an opinion as to its value. The acrosclerotic type of scleroderma is by far the most common in our practice and seems definitely related to Raynaud's phenomena, because when the patient no longer has the vasospastic attacks, the cutaneous sclerosis tends to fade out and disappear. This results in an almost normal-appearing skin but with a loss of the subcutaneous tissue, of which the peach pit chin is a classical example. Absorption of the terminal phalanges, shortening of the esophagus, and x-ray evidence of pulmonary fibrosis are manifestations of this phase of the disease, in which the cutaneous sclerosis is also conspicuous because of its absence. In both morphea and acrosclerosis, spontaneous involution occur, while in generalized or systemic scleroderma, involution seldom if ever takes place.

DR. JAMES R. WEBSTER, Chicago: Just a comment on the patient with ulcerations and bullae, because I have recently seen a patient in Chicago who had this same picture only very much more pronounced in all its manifestations, very much more extensive than this lady had. My patient also had a great many bullous lesions, although I was of the impression that they were more localized—breakdown of tissue—than any this patient had. My patient was extremely obese and had striae, as this patient had. X-rays were negative. There was no pituitary involvement. I feel that an individual with an extensive morphea of the skin might very well be more susceptible to a breakdown from trauma, etc. I think it is unusual to see bullae.

Peyronie's Disease. Presented by ANCKER HOSPITAL STAFF.
Peyronie's Disease. Presented by ANCKER HOSPITAL STAFF.
Xanthoma. Presented by DR. ORVILLE E. OCKULY.
Necrobiosis Lipoidica Diabeticorum. Presented by DR. ORVILLE E. OCKULY.
Necrobiosis Lipoidica Diabeticorum. Presented by DR. ORVILLE E. OCKULY.
Acrodermatitis Atrophicans Chronica. Presented by ANCKER HOSPITAL STAFF.
Vitiligo. Improvement Following Thyroidectomy. Presented by DR. JOHN F. MADDEN.
Argyria. Presented by ANCKER HOSPITAL STAFF.
Dermatitis Herpetiformis or Pemphigus Vulgaris. Presented by DR. JOHN F. MADDEN.
Marfan's Syndrome (Arachnodactyly with Blue Sclerae). Presented by ANCKER HOSPITAL STAFF.
Acne of Face—Precocious Puberty. Presented by ANCKER HOSPITAL STAFF.
Reiter's Syndrome. Presented by DR. HAROLD G. RAVITS.
Parapsoriasis en Plaque. Presented by ANCKER HOSPITAL STAFF.
Neurofibromatosis. Presented by ANCKER HOSPITAL STAFF.
Neurofibromatosis. Presented by ANCKER HOSPITAL STAFF.
Ichthyosis Hystrix. Presented by DR. JOHN F. MADDEN.
Ichthyosis Hystrix and Bowen's Disease of Sacral Area. Presented by ANCKER HOSPITAL STAFF.
Plantar Wart. Presented by ANCKER HOSPITAL STAFF.
Callositas. Presented by ANCKER HOSPITAL STAFF.
Keratoderma Palmaris et Plantaris. Presented by DR. JOHN F. MADDEN.
Acute Disseminated Lupus Erythematosus. Presented by UNIVERSITY HOSPITAL STAFF.

NEW YORK DERMATOLOGICAL SOCIETY

George C. Andrews, M.D., *President*

Gerald F. Machacek, M.D., *Secretary*

Jan. 26, 1954

Dermatitis Herpetiformis Treated Successfully with Promacetin. Presented by DR. MAURICE J. COSTELLO.

P. G., a man aged 58, has had typical dermatitis herpetiformis for 20 years. The eruption was extremely pruritic, with many exacerbations and partial remissions. On several occasions he has had mouth lesions. When I first examined him he had numerous grouped, discrete, excoriated, erythematous, matchhead- to pea-sized papules and papulovesicles. On Dec. 14, 1953, Promacetin (sodium 4,4'-diaminodiphenylsulfone-2-acetylsulfonamide) 1.0 gm., t.i.d., p.c. was administered. Even though the patient had mild toxic manifestations from the drug, such as diarrhea and head-

ache, the eruption disappeared in one week under this therapy. The disease was finally controlled with 0.5 gm. t.i.d. The urine was normal, and the complete blood cell count was normal except for 46% lymphocytes.

DISCUSSION

DR. GEORGE C. ANDREWS: Since Dr. Costello mentioned that type of treatment to me I have used it on several patients with excellent results. I feel as he does that it is less toxic than sulfapyridine and gives an excellent result.

DR. MAURICE J. COSTELLO: I have treated at least nine cases with Promacetin. Several patients who had been controlled with sulfapyridine for eight and nine years were later controlled by Promacetin, which is less toxic than the former and I am inclined to think just as effective in most cases. I have seen dermatitis medicamentosa follow the administration of Promacetin.

DR. GEORGE C. ANDREWS: It produced a toxic morbilliform eruption in one of my patients.

Microaerophilic Hemolytic Streptococcus Infection (Meleney). Presented by DR. EUGENE F. TRAUB.

P. S., a woman aged 37, noticed a small lesion on the lower central abdominal wall about 14 months ago, and thought it was a "boil." The lesion spread peripherally in all directions and enlarged into a flat, vegetative, marginated ulcer. This was surgically excised, and a long, healed transverse scar marks the site. The excision healed nicely, except that on the left-hand corner a small lesion appeared, which rapidly enlarged and is now assuming an appearance similar to that of the original ulceration. More recently another such lesion has appeared on the right side of the abdomen, but it has not grown rapidly. Within the past month an entirely new lesion has appeared just below and about the lobe of the left ear. This is now characterized by deep, ragged ulceration, with some hypertrophic areas in the center. Innumerable cultures have been taken, and the chief growth has been Proteus vulgaris, which no doubt is responsible for the foul odor emanating from the lesions and also possibly the watery discharge. In cultures grown under anaerobic conditions in a special medium of beef extract broth with 10% blood serum, a hemolytic Streptococcus has been isolated. Serologic examinations have been normal. The cultures have not grown fungi at any time.

There is no history of drug ingestion.

Six x-ray treatments were given with no benefit. All types of antibiotics were pushed to extremes without influence. The present treatment is the application of fresh zinc peroxide.

DISCUSSION

DR. GERALD F. MACHACEK: It is an unusual but very grave problem, because the process may go on and on and the patient may finally die. I don't think calling it an ulcer answers the question. It is more sphaceloderma, pyoderma gangrenosum. We should look for other etiologic factors, such as beryllium. Some form of heat or ultraviolet therapy should be used locally. It is difficult to outline a way of attacking this problem, but it can prove very serious.

DR. GEORGE C. ANDREWS: I agree with Dr. Machacek that it is a grave problem. I see no clinical reason to disagree with the diagnosis but think further search should be made for other factors and the reason why the woman's resistance is as low as it is to these organisms. On account of these deep, intertwining sinuses which keep draining pus, one must search farther for blastomycosis and other deep fungous infections. I would also consider giving her further internal treatment. If all the antibiotics have been used without effect, one might think of diethylstilbestrol, or one of the nitrostyrenes used by Arthur Curtis for blastomycosis. There is also the possibility that blood transfusions might help. We had a patient die at the Medical Center of this disease—a big, strong man who looked in perfect health, with no evidences of focal infection or other ascertainable causes. Has this woman had corticotropin (ACTH) or cortisone? Someone reported a cure of gangrenous stomatitis and granuloma gangrenescens in that way.

DR. GEORGE M. LEWIS: Blastomycosis would be unlikely because the border of the lesion does not slope and is entirely free of small miliary pustules. I wonder whether vaccine therapy would be of any help? We have come to rely so much on chemotherapy that we are in danger of forgetting some of the older therapies.

DR. FRANK E. CORMIA: If the patient doesn't respond to zinc peroxide, bacitracin-neomycin (Bacimycin) might have a local sterilizing effect. I believe vaccines have been used, but not successfully, as patients do not develop an adequate antibody response.

DR. HERBERT J. SPOOR (by invitation): Isolation of the organism as recommended by Meleney is a rather difficult technique; it not only requires that blood be present in the nutrient medium, but also there must be true anaerobic conditions. One can't use thioglycollate only. We managed to get the Streptococcus out first by using an atmosphere of carbon dioxide, but even then after 24 hours there was an overgrowth of Proteus. The difficulty is that Proteus overgrows everything, even in fungus media.

A Case for Diagnosis (Dermatitis Herpetiformis; Impetigo Herpetiformis?) Presented by DR. ANTHONY C. CIPOLLARO.

A. K., a man aged 51, has had a chronic vesiculopustular eruption characterized by remissions and exacerbations, for the past two and a half years. The remissions are never complete and last from four to six months. The exacerbations are usually of four to six weeks' duration, but the present attack, which has lasted six weeks, is more severe and extensive than any of the preceding ones. The original lesions two and a half years ago appeared in the groin. The present attack was more explosive and generalized at the start. The primary lesion is a vesicle or pustule which is pruritic and easily ruptures, with the formation of thick brown crusts. New lesions appear adjacent to the original one, coalesce and advance peripherally in a serpiginous manner. At present, in addition to pruritis, there is severe burning. The disease is still active, new lesions appearing daily.

Four months ago the patient developed a pleuritic pain in the right side of the chest which was found to be secondary to thrombophlebitis of the right thigh. The embolic area cleared rapidly, but the thigh became increasingly tender and edematous and finally a large slough developed. This was grafted two and a half months ago with a 90% take, but in the past few weeks several ulcers have appeared in the recipient site. The patient has also had arthritis for the past three years, involving mainly the shoulders and fingers, with occasional involvement of the knee joint. This has been treated with gold and salicylates.

There are discrete, erythematous, vesiculopustular lesions in the axillae, groin, cubital and popliteal fossae, and scattered over the trunk. On the trunk and extremities there are grouped vesicles and pustules arranged in crescentic and gyrate figures with advancing, serpiginous borders. There is a considerable inflammatory reaction around these lesions. There are large areas of hyperpigmented skin representing previously involved sites. The recipient site on the posterior surface of the right thigh measures 5 by 8 in. (12.7 by 20.3 cm.). Within the graft area there are four deep, punched-out ulcers with clean bases measuring from ½ to 1½ in. (1.3 to 3.8 cm.) in diameter.

Blood count showed hemoglobin 13 gm. per 100 cc., red blood cells 4,500,000, and white blood cells 9,050, with polymorphonuclear leucocytes 62%, stab forms 10%, lymphocytes 27%, and eosinophiles 1%. Urinalysis was normal. The blood sugar was 66 mg., nonprotein nitrogen 51 mg., and total protein 7 mg. per 100 cc., with albumin 4.6 and globulin 2.4 gm. per 100 cc.

Treatment in the past has consisted of sulfapyridine, potassium permanganate baths, and emulsions. For the past five weeks the patient has received 150 mg. of cortisone daily, with 40 units of corticotropin (Acthar) gel weekly. The steroid therapy is being gradually withdrawn. Promacetin, 2 gm. daily, was begun two days ago, and calamine lotion with 1% phenol is being used locally.

DISCUSSION

DR. GEORGE M. LEWIS: Dermatitis herpetiformis would appear to be the most likely diagnosis at this time. I can't see any clinical support for pemphigus, although it cannot be entirely ruled out as a possibility.

DR. WILBERT SACHS: I agree with those who feel it is clinically dermatitis herpetiformis, and yet I couldn't make this diagnosis microscopically. There was something in that slide to suggest the possibility of pemphigus, and there are some features clinically to suggest this disease also. I suggest that pemphigus be considered as a possibility.

DR. PAUL E. BECHET: The evidence against impetigo herpetiformis is sufficient to disqualify that diagnosis for the following reasons: The patient is male; while cases have been

reported in men by Kaposi, Dubreuilh, Whitehouse, and Chambers, the overwhelming majority of victims of this disease are women during pregnancy or the puerperal period. Almost all patients evidence severe constitutional symptoms which frequently end fatally, whereas this man is not apparently seriously ill. The markedly circinate configuration of the lesions, while common in impetigo herpetiformis, is also frequently observed in dermatitis herpetiformis. In my opinion, therefore, the clinical evidence favors the latter.

DR. GEORGE C. ANDREWS: I realize that dermatitis herpetiformis is probably the clinical diagnosis, but like Dr. Sachs I would have my reservations about it. This is just too bizarre an example of a configurate eruption for me to be perfectly satisfied with that diagnosis. I still think that pemphigus is a possibility because of the fact that the man says he gets blisters on the lips and front part of the mouth. Those may be just herpes, but he made that statement. Just as a matter of routine I think fungous infection should be excluded.

DR. WILBERT SACHS: This was an intraepidermic bulla, and that is why we thought it was probably pemphigus.

DR. EUGENE F. TRAUB: The patient has been followed a good many years. The sulfonamides have been used with no response, and local remedies have been employed. I would say it was likely to be a case of pemphigus.

DR. MAURICE J. COSTELLO: I have seen this polycyclic eruption in pemphigus, dermatitis herpetiformis, and erythema multiforme, though it is more likely to occur in the last. The fact that he has had it for three years, that he had an infection on the back of the right leg, and has not lost weight, strength, or appetite I think would be against pemphigus. The lesions begin as vesicles, soon become pustules, and then spread peripherally. I would be inclined to think it is dermatitis herpetiformis, and that he should have a good trial of Promacetin.

DR. ANTHONY C. CIPOLLARO: I am a little disappointed that no one mentioned drug eruption. The patient has been taking acetylsalicylic acid for rheumatism for years. I shall probably go along with Duhring's disease, drop the cortisone, and continue the Pomacetin which was begun yesterday.

Report from Meeting of Nov. 24, 1953

Case for Diagnosis (Nevoxanthoendothelioma? Urticaria Pigmentosa?). Presented by DR. GEORGE M. LEWIS.

DR. GEORGE M. LEWIS: A biopsy confirmed the diagnosis of nevoxanthoendothelioma.

Gaucher's Disease with Collagen Disease (Rheumatoid Arthritis?). Presented by DR. GEORGE C. ANDREWS.
Lepromatous Leprosy. Presented by DR. MAURICE J. COSTELLO.
Tuberculoid Leprosy. Presented by DR. MAURICE J. COSTELLO.
Case for Diagnosis (Acanthomas?). Presented by DR. EUGENE F. TRAUB.
Contact Dermatitis Due to Rubber Cement in Shoes. Presented by GEORGE C. ANDREWS.
Recurrent Basal Cell Carcinoma. Presented by DR. FRANK E. CORMIA.
Erysipelas-Like Dermatophytid. Presented by DR. EUGENE F. TRAUB.
Case for Diagnosis (Mycosis Fungoides?). Presented by DR. EUGENE F. TRAUB.

Obituaries

MARTIN FEENEY ENGMAN SR., M.D.
1869-1953

MARTIN FEENEY ENGMAN SR., at the age of 85, died on Oct. 12, 1953. His name will always remain among the outstandirg men in dermatology in this country.

A contemporary of Pusey, Pollitzer, Haase, Wende, Ormsby, Guy Lane, and Schamberg, he was one of that group of leaders who raised the infant specialty of dermatology to maturity. Dr. Engman lives in the hearts of the men he trained and in the thoughts of the sick and suffering he helped while in the wards and clinics of the Barnard Free Skin and Cancer Hospital and the Barnes Hospital in St. Louis, and in the United States Public Health Hospital (the National Leprosarium) at Carville, La.

Dr. Engman was a great diagnostician and a teacher whose clinics were well attended by his students because he created in them a great interest in dermatology.

The partnership of Engman and Mook endured for many years, as he and Mook were the closest of friends and were almost like brothers. It was a combination of two unusual personalities with exceptional talents.

Dr. Engman was one of the first physicians in this country to use the arsphenamines. Ehrlich sent some of the drug, and Engman readily demonstrated its value in patients with syphilis.

Dr. Engman instigated the expansion of the National Leprosarium at Carville, La., with the help of Surgeon General Sternberg, and Senators Ransdell and Reed. These efforts were well rewarded in that they resulted in the provision of adequate facilities for the care of lepers in one of the world's leading leprosariums.

Dr. Engman also pioneered x-ray and radium therapy in St. Louis and established at the Barnard Free Skin and Cancer Hospital a weekly radium conference.

Dr. Engman founded the Barnard Free Skin and Cancer Hospital. The St. Louis tornado of 1897 caused great destruction in the City Hospital, so temporary quarters for the city's indigent sick were secured at the House of the Good Shepherd. As the facilities there were inadequate, he gathered together a group of St. Louis doctors and financial leaders and secured contributions to start a skin and cancer hospital. The small institution was supported by private contributions for several years, until it finally attracted the attention of Mr. George Barnard, who gave several thousand dollars toward the maintenance fund. Subsequently Mr. Barnard gave the St. Louis Skin and Cancer Hospital a new building, which is named after him.

Shortly after the new building was occupied, Mr. Charles H. Huttig, then president of the Board of Directors, started a drive for an endowment fund. Charitable women of the City of St. Louis raised a sum of more than twenty thousand dollars which was added to the nucleus of the endowment fund origi-

nally subscribed to by the members of the Board of Directors and other benevolent citizens. This capital fund is inviolable. The yield on it is used for the care and maintenance of patients in the hospital. Also Mr. Barnard bequeathed a large sum of money for the maintenance of the hospital and for the care of its patients.

Among many of Dr. Engman's accomplishments was the demonstration of the role of Staphylococcus in impetigo; with Mook, he demonstrated the fragmentation and loss of elastic tissue in epidermolysis bullosum. He was one of the first to describe bullous lichen planus. With Heithouse, he described the first United States cases of amebic skin infection. His interest in pellagra was intense, and he was called by Goldberger to confirm the diagnosis in the experimental lesions

MARTIN FEENEY ENGMAN Sr., M.D.
1869-1953

which the latter had produced on the skins of Mississippi convicts by vitamin-free diets. He was a pioneer in the treatment of skin cancer and angioma with radium. He described infectious eczematoid dermatitis and hereditary pigmentation of the skin of the legs.

He worked with Kendall on some of the phases of the discovery of the thyroid hormones, and some of his unfinished work with one of Kendall's thyroid fractions might well be continued today.

He was one of the first to use liquid oxygen in the treatment of skin lesions. He very early recognized the role of allergy in the production of skin diseases, and some of his early work on drug eruptions can still be read with great profit.

His knowledge of what today is a vanishing disease, viz., syphilis, was profound and he contributed much to the clinical interpretation of serological reactions both on the blood and on the spinal fluid.

He was profoundly impressed with the work of Dale and Laidlaw with histamine and predicted that histamine or related substances were responsible for urticarial phenomena.

Dr. Engman was a student of history and used historical points at times to illustrate his lectures. He was a hard taskmaster. He insisted that his students study, work, and produce. Not that he wanted them to produce papers for the sake of publishing something, but because he wanted them to investigate a phase of some skin problem and record what they had learned so that others might benefit by their efforts. When, however, one of them did produce something good, he was proud and pleased. His smile of approval and the laughing twinkle in his eye were a delightful reward for hard work and worth-while accomplishment.

Dr. Engman is survived by his wife, two sons, Dr. Martin F. Engman Jr. and Walter C. Engman, and a sister, Mrs. Tillie Engman Stoll of South Bend, Ind. He was a happy grandfather and took great pleasure in his three sturdy grandchildren. He was a member of the Episcopal Church. His thoughts on religion were broad and tolerant.

When we contemplate the end of a long and useful life, a life devoted to the service of mankind, of course we grieve that such a man must go. But we all must go sooner or later, and if we can leave such a record of service, then we can be satisfied.

For a doctor can do no better than to devote his life to alleviate suffering and to add his contributions to the understanding of disease. Dr. Engman was such a man. His colleagues, his patients, and his students will long remember him. His family can be proud of such a husband and father.

Richard S. Weiss, M.D.

JOHN EDWARD RAUSCHKOLB, M.D.
1895-1954

JOHN EDWARD RAUSCHKOLB was born in Columbus, Ohio, Oct. 19, 1895, the son of John Rauschkolb, M.D., and Edith Ritson. After beginning professional life as a pharmacist, his father studied medicine and graduated from the old Starling Medical College in Columbus in 1898, later lecturing on pharmacy at his alma mater. A capable and highly respected physician, he was past-president of the Columbus Academy of Medicine and continued in practice until his death, from cerebral hemorrhage, at the age of 80. His wife lived to be 93. So their son might reasonably have anticipated a fairly long life.

John Edward Rauschkolb entered the Liberal Arts College of Ohio State University. His academic career was interrupted by military service, first with the Ohio National Guard on the Mexican border and then in the United States Army in France. He was attached to the 112th Sanitary Train, 146 Field Hospital of the 37th Division, serving as a first sergeant in France and Belgium in many of the major engagements of World War I. For this he received the Silver Star decoration.

Returning to Ohio State University after the war, he obtained his A.B. degree in 1920 and then entered the School of Medicine of Western Reserve University, which granted him an M.D. degree in 1923. Both his internship and his residency were at the Cleveland City Hospital. This hospital and his medical alma mater he served continuously with a high degree of fidelity until his life's end. His appointments in the School of Medicine were as follows: demonstrator of dermatology, 1925-1926; instructor in dermatology and syphilology, 1926-1928; senior clinical instructor, 1928-1930; assistant clinical professor, 1930-1954. He was in active personal charge of the large and very active outpatient and inpatient departments at Cleveland City Hospital, acting as assistant department head. The inpatient service, with about fifty hospital beds, was one of the largest in the country at that time. After the resignation of Dr. Harold N. Cole in 1952, he became the department head. Here and elsewhere his genius for organization was made evident. His presentations of patients at clinical sessions of the local, regional, and national dermatological meetings held in Cleveland were models of accuracy, thoroughness, and completeness.

In 1926 he was married to Ruth A. Robishaw, M.D., a medical school classmate. They shared large and especially well equipped offices for many years, Dr. Robishaw limiting herself to internal medicine until two years ago, when she began the study of dermatology, expecting to practice with her husband. They have two children, Elizabeth, a freshman student in the School of Medicine of Western Reserve University, and Diana, a senior at Wellesley College.

The Rauschkolbs traveled extensively in both North and South America, Europe, and Hawaii. Most of these journeys were primarily for the purpose of attending medical meetings, including the International Congresses in Dermatology in Copen-

hagen in 1930 (where Dr. Rauschkolb had an exhibit on chancroids in the venerology section) and in London in 1952. A founding member of the American Legion, he attended its 1937 meeting in Paris.

John had a genuine liking for people and an inborn desire to serve them. In the thirties and early forties he was active in the work of the Cleveland Academy of Medicine and was president in 1942-1943. He was also president of the Cleveland Dermatological Society in 1936-1937.

The American Academy of Dermatology and Syphilology was fortunate enough to enlist his services. He participated frequently in its teaching program, and in 1948 became assistant secretary-treasurer under Dr. Earl D. Osborne, whom he succeeded as secretary-treasurer in 1950. Owing to his administrative skill, friendliness, and untiring energy, the smooth operations of this complex teaching organization were continued most effectively.

As would be expected with one endowed with such a warm personality, he was a member of several of Cleveland's leading social clubs and was also a thirty-second degree Mason and a Shriner.

Noted for his tolerance and broad human sympathy, he was interested in the formation of the new interracial Forest City Hospital in Cleveland and served as chairman of its executive committee. He was chief consultant in dermatology and syphilology at the Evangelical Deaconess Hospital and head of the department of dermatology and syphilology at St. Alexis Hospital. As one of the founders' group in 1933, he was a specialist certified by the American Board of Dermatology and Syphilology and was a member of many medical organizations in addition to those mentioned above, including the American Dermatological Association, the Society of Investigative Dermatology, the American College of Physicians, the Central States Dermatological Society, the Cleveland Medical Library Association, the American Medical Association, and its constituent county and state units.

Endowed with a rugged constitution, he had always enjoyed the best of health, but early in March suffered a severe upper respiratory tract infection caused by a nephrotoxic strain of streptococci. Acute glomerular nephritis resulted, and he passed away, April 28, 1954. At memorial services held in the auditorium of the Cleveland Medical Library Association on Saturday, May 1, 1954, a large number of Cleveland physicians with dermatologists from other cities gathered to pay tribute to a dearly beloved friend, a valiant worker for the common welfare, and a most worthy disciple of the healing art.

CLYDE L. CUMMER, M.D.

Books

Dermatology: Essentials of Diagnosis and Treatment. By Marion B. Sulzberger and Jack Wolf. Price, $10.00. Pp. 592, with 65 illustrations. The Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1952.

This book is a revision of these authors' previous text, "Dermatologic Therapy in General Practice." As was true in the past, this present edition represents a compendium rather than a complete dermatologic text.

The subjects considered are those most commonly seen in a dermatologic practice. Adequate descriptions of the various entities are included along with a multitude of suggestions for their treatment. The beginner may be confused rather than enlightened by the number of therapeutic suggestions.

The text contains a dearth of clinical pictures. To the novice in dermatology, the following proverb is apropos: "One picture is worth a thousand words." It is to be hoped that in future editions, more pictures may be added. Included are eight colored plates reproduced from Ciba: "Clinical Symposia" and these are excellent for their color qualities and reproduction of details.

The general practitioner and medical student will find this book of value in orienting themselves to the field of dermatology. Because its scope is so limited, the graduate student in dermatology can consider it hardly more than an introduction to this specialty.

Dermatologie. By Robert Degos, Professor, Clinic of Dermatology and Syphilology, Faculty of Medicine, Saint-Louis Hospital, Paris. 8,600 fr. pp. 1124, with 301 illustrations. Ernest Flammarion, 22 Rue de Vaugirard, Paris, 6e, 1953.

This book is a very good indication of the persistent vitality and dynamism of the old Dermatological School connected with the famous Hôpital Saint-Louis of Paris. The author is a well-known dermatologist, having been a pupil of Gougerot before becoming chief of one of the five dermatological services of that hospital. From his manifold experience in the clinic and in teaching, covering two decades, he was able to draw an abundance of interesting material for this well-balanced, clear, and up-to-date textbook. He omits the preliminary general information about anatomy, chemistry, and physiology, but he covers the entire field of dermatology with the usual clarity of the Gallic mind. His clinical sketches, short historical notes, and brief but adequate histological descriptions are matched only by the most recent therapy, which includes the antibiotics, the steroids, the quinacrine (Atabrine) and chloroquine treatment of discoid lupus erythematosus, etc. The text is, furthermore, interspersed with numerous beautiful, black and white clinical and pathological illustrations. There is little to which one can take exception. Indeed "Dermatologie" will prove to be an enjoyable companion and a valuable reference book for anyone having at least a reading knowledge of French. The format of the book is of the fly-leaf type, as the author expects to revise and add to the text every year, in keeping with the dynamic evolution of modern dermatology.

Veterinary Dermatology. By Frank Kral and Benjamin J. Novak. Price, $10.00. Pp. 325, with 162 illustrations. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5, 1953.

This publication distinguishes itself by being the first complete text on skin diseases in animals to be published in English. Its spectrum of interest is broadened by the transmissibility of many animal dermatologic entities to man and by the stimulation of thought toward supplemental animal research by pointing out the advantages and disadvantages of various animals in the evaluation of dermatologic problems. An interesting comparison of sweat mechanism dissimilarities in various animals and man offers avenues for further advancement in the study of sweat physiology. A worth-while discussion of hyper- and hypopigmentation is presented; it includes a note on acanthosis nigricans in dogs. The sections on virus diseases, parasitic infestations, and infectious diseases in general are well done. The unfamiliar veterinary nomenclature

without glossary and the frequent lack of correlation of terminology with that used in human dermatologic texts raises the question as to the advantages which might be gained by the collaboration of a dermatologist in the preparation of such a text. The book bears out the cliché that humans aren't very different from animals; they both scratch when they itch.

Histopathology of the Skin. Second Edition. By Walter F. Lever, M.D. Price, $12.00. Pp. 518, with 281 illustrations. J. B. Lippincott Company, E. Washington Square, Philadelphia 5, 1954.

Much credit is due Dr. Lever for his excellent textbook on dermal histopathology. The second edition has been rather extensively revised and brought up to date. Several new subjects and new concepts have been added, while some of the old material has been rearranged and shortened. The number of pages in the book has been increased, in part through added microphotographs. Among the chapters most extensively revised are those on vesiculobullous diseases, nevimelanomas, the purpuras, and metabolic diseases. Several new entities have been added, such as benign and malignant hibernoma, lupus erythematosus profundus, and the progerias, to mention a few.

There are several features that are controversial, such as listing lichen sclerosus et atrophicus under the heading of kraurosis and the statement that pustular lesions do not occur in psoriasis.

The book is somewhat dogmatic, but at least for beginners in the field of dermatopathology this is probably an advantage. The book is highly recommended to both the beginner and the advanced student in histopathology of the skin.

Affections de la chevelure et du cuir chevelu: anatomie, physiologie, pathologie, hygiène et thérapeutique. By A. Boutelier and others; edited by A. Desaux. Price, 5,650 francs. Pp. 780, with 298 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1953.

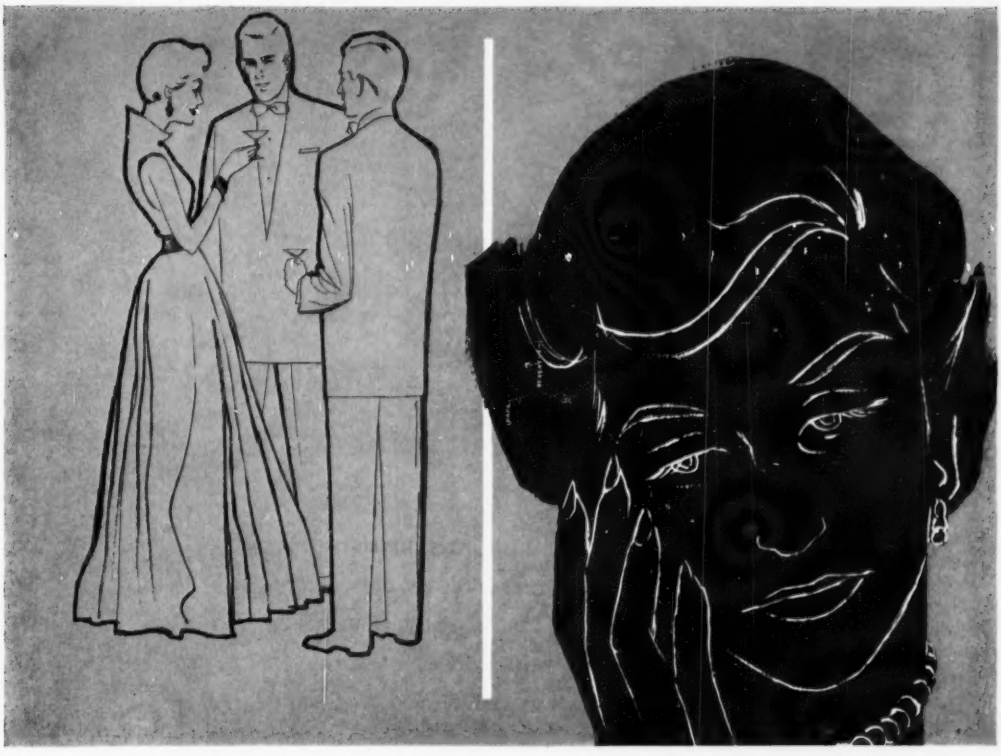
This is a comprehensive work by 14 collaborators on diseases of the scalp and the hair. All of the contributors are authorities on the subjects assigned to them.

The volume consists of 780 pages, with an excellent index and voluminous references, printed on the very best grade of paper and beautifully bound. The illustrations, many of which have been taken from "Nouvelle Pratique Dermatologique," are excellent. During several conversations, on his recent visit to the United States, Desaux expressed to this reviewer his regret that the subscribers for the French journals were so few in the United States. It was explained to him that no longer is a reading knowledge of French and German required in the premedical courses and that it is no longer necessary for medical men to go to Europe for postgraduate training. It is therefore most unfortunate, indeed, that this very valuable work will be read by so few, unless an English translation be made.

Every conceivable phase of this subject of diseases of the scalp and of the hair has been thoroughly explored, and it is, as of the present, a work not soon to be surpassed.

The last chapter in the volume, by Verdeaux, entitled "Psychopathologie du cuir chevelu," takes us back to prehistoric days and brings us up to date on all of the beliefs and superstitions about the hair. This chapter is not only informative, but is also delightfully presented.

An English translation would be welcomed by the English-speaking world.



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Archives of Otolaryngology, Sept. 1952: 241-249
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Archives of Otolaryngology, March 1947: 294-297
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References:

1. Ellis, C. C., and others: The Treatment of Psoriasis with Liquor Carbonis Detergens, J Invest. Dermat. *10*:455, 1948.

2. Sulzberger, M. B., and Wolf, J.: Dermatology. Essentials of Diagnosis and Treatment, Chicago, Year Book Publishers, Inc., 1952, p. 323.

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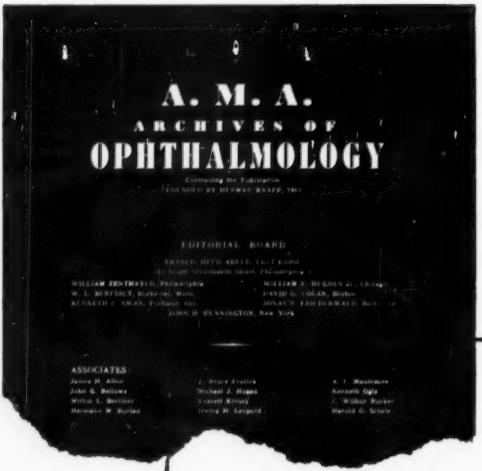

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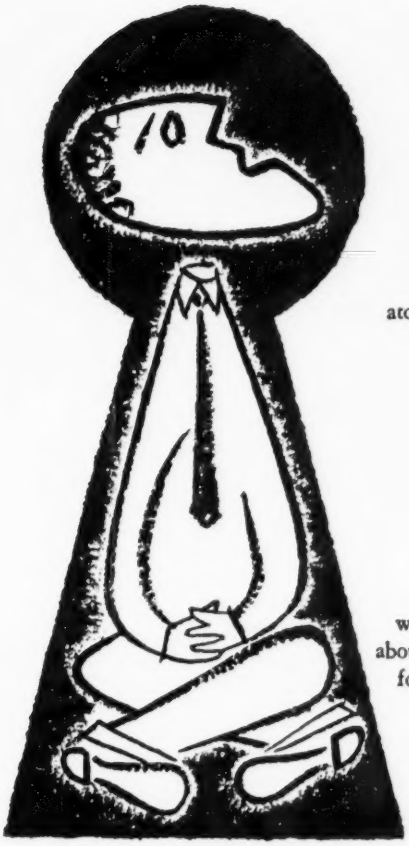

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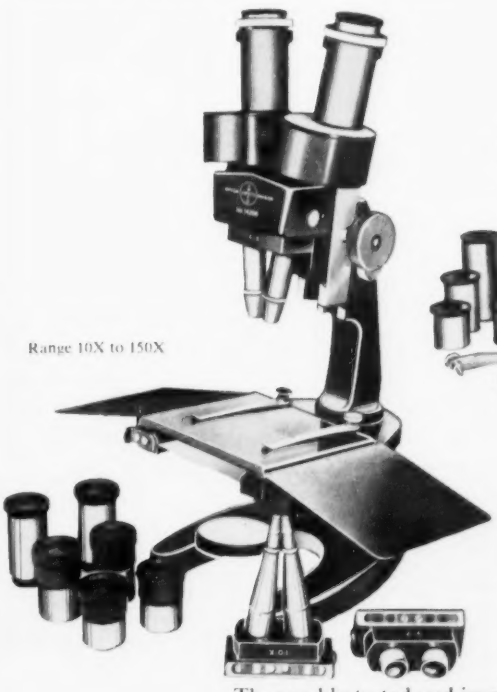

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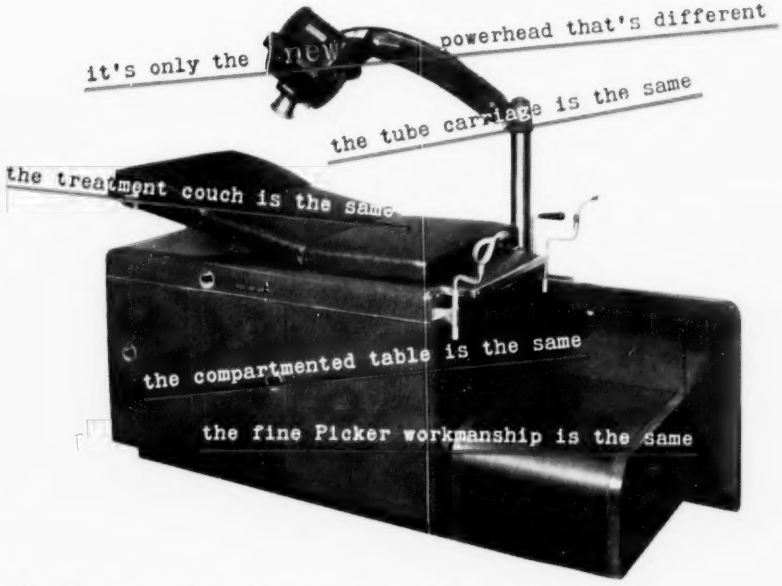
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